Adiposis Dolorosa Is More Than Painful Fat

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Objective: To describe signs and symptoms of adiposis dolorosa (AD) in a large cohort of individuals with this disorder to increase recognition, diagnosis, and research of this syndrome.

Design: Survey.

Subjects: One hundred ten men and women with AD.

Measurements: The survey included questions on demographics, obesity, signs and symptoms in soft tissues and body systems, susceptibility to infection, diet, treatments and lifestyles, medical and family history, habits, and exercise.

Results: Subjects were white, non-Hispanic except for 3 Hispanics and 2 African Americans, and mostly women (82.7%) of northern European ancestry living in the United States (87.3%), average age 48.5 ± 10 years. The majority of respondents were obese, body-mass index of 34.7 ± 8.7 kg/m² and had AD for 14.5 ± 11.9 years. Onset of growths began primarily in the arm or leg at a mean age of 34.5 ± 12.8 years (range, 7–67 years). The majority reported pain, fatigue, weight gain (25.7 ± 15 kg), multiple growths, and weakness at onset. The median number of palpable growths was 77.3 ± 84.5 in subcutaneous fat from scalp to dorsal foot. Growths ranged from firm and pea-sized to large, fixed, and deep. Pathology descriptions of growths included lipoma, fibrolipoma, or angiolipomas. Autoimmune disease and fibromyalgia were prominent (38.2%), as was diabetes (16.4%). Almost all respondents reported exercise-associated pain in growths, and 100% saw no decrease in growths with weight loss. Over 75% had liposuction and over half reported regrowth. Almost half reported family members with growths.

Conclusion: Our survey results suggest AD is a painful syndrome involving growths in all subcutaneous fat. It can be inherited or sporadic, beginning in the third decade of life, but can occur in children and is accompanied by obesity, fatigue, joint and muscle aches, and other signs and symptoms affecting multiple organ systems. Exercise induces pain and has no effect on fatty growth size. The etiology of this syndrome remains unknown.

Key Words: Dercum disease, painful fat, adiposis dolorosa, lipomatosis, obesity

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Learning Objectives

- Summarize the demographic features of the 110 patients with adiposis dolorosa (AD) in this study; the onset and course of the disorder; and the characteristic symptoms and signs.
- Give examples of the broad range of conditions associated with AD.
- Identify the modes of treatment undertaken by these patients and those that seemed most effective.

Dercum described adiposis dolorosa (AD) in 1888 as painful growths in subcutaneous fat that can be pea-sized or pendulous. The onset of AD is insidious and progressive, associated pain and fatigue disabling, and pain unresponsive to analgesics. Obesity is common in AD, with some describing rapid weight gain. Some cases of AD are familial. The etiology of AD is unknown, although metabolic or autoimmune components have been proposed. AD is listed by the National Organization for Rare Disorders, Inc, but in Sweden, the prevalence is 0.1%; it is thought to be at least 5 times more common in women but rare in children. Kling described 112 cases of women with juxta-articular AD, suggesting its commonality, but patients with AD can be dismissed as malingerers with emotional problems. Growths can appear overnight or morph shape in real time, which might contribute to disbelief of AD among medical care providers. There is little recent information on AD except an on-line paper and case studies. Using published data and discussions among patients with...
AD, we designed a questionnaire and surveyed 110 individuals with AD to better understand this virtually unexplored syndrome of focal obesity and increase its recognition by healthcare providers.

METHODS

Survey Description
The survey was based on published data\textsuperscript{1,2,5,6} and conversations with patients diagnosed with AD. The survey was sent by e-mail or postal mail from March-December 2006 to persons requesting the survey after advertisement through an online support group.\textsuperscript{15} The survey consisted of questions on demographics, growths, muscle, blood vessels and nerve symptomatology, obesity, skin, susceptibility to infection and associated tumors, a checkbox table on treatments and lifestyles and their effect on growths, a table of 36 symptoms graded by frequency from 1 to 5 (1 = never; 2 = once a month; 3 = 2–4 times a month; 4 = 5–7 times a month; 5 = daily), and sections on medical history, family history, diet, habits, and exercise. Respondents were \textgreater 18 years and diagnosed with AD. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. Procedures were approved by the University of California San Diego institutional review board. All subjects provided informed consent before completing the survey.

Survey Disposition
There were 358 members of the on-line support group\textsuperscript{15} by the end of recruitment who were contacted by e-mail. The disposition and disposition codes\textsuperscript{16} (in parentheses) are as follows: 20 individuals were excluded because they did not have AD (4.10); 6 individuals were excluded because their responses arrived late (4.80); 15 e-mails were returned undelivered (3.30); 16 individuals were contacted and provided a survey but did not return it (2.20); 191 never replied to the e-mail or returned a questionnaire (3.19); and 110 individuals completed the survey within the recruitment period and were enrolled (1.1). The response rate was 34.7%, the cooperation rate of responders 100%, the refusal rate of responders 0%, and the contact rate 87.3%.

Statistics
Data are percent of respondents, or average \pm SD. Differences between groups were by Student \textit{t} test and correlation was by Pearson product moment correlation, using SigmaStat Software (Jandel Scientific Software, San Rafael, CA, US).

RESULTS

Demographics
All 110 subjects who completed the survey were white and non-Hispanic except for 3 white Hispanics (1 man and 2 women) and 2 African Americans (a man and woman); 20 subjects were part American Indian (18.2% Table 1). There was no significant difference for age, sex, or body-mass index (BMI) between international and US respondents; therefore, data were pooled. The average age of respondents was 48.5 \pm 10.1 years (range, 21–76 years). A majority of respondents were women (82.7%) living in the United States (87.3%) who

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<th>TABLE 1. Demographics of Subjects With AD</th>
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were unable to work secondary to AD (56.4%). The cultural ancestry of respondents was Irish (36.4%), German (33.6%), Scottish (20%), French (14.5%), Polish (9.1%), Italian (6.4%), or Swedish (5.5%), with additional heritages <5% of respondents.

Onset of AD

The average age of onset of growths was 34.5 ± 12.7 years (range, 7–76 years). Many women (85.7%) developed AD before menopause. Forty-two percent of men and 8.8% of women were children when they developed AD (≤18 years of age; Fig. 1). The average duration of AD was 14.5 ± 11.9 years, with a median of 10.5 years and range of 1–45 years. Growths were first noticed on the leg (30.9%), arm (23.6%), rib cage, chest or breast (14.6%), back (10.9%), abdomen (13.6%), neck (4.6%), buttck (1.8%), and forehead (1.8%). Over half (55.5%) experienced multiple growths at the initial or additional site at onset of AD. Symptoms and signs at the initial site of growth(s) included pain (83.6%), burning (43.6%), stiffness of soft tissue or joint (38.2%), bruising (31.8%), itching (28.2%) and a papule (4.5%). Weight gain at AD onset was reported by 53.6% of the respondents and ultimately occurred in 89.1%, gaining on average 25.7 ± 15.6 kg (median, 22.7 kg; range, 2.3–65.2 kg). However, 30% of respondents also reported a past history of large weight loss or anorexia; therefore, in some, weight gain could be weight regain. Major complaints at the onset of growths included fatigue (71.8%), weakness (48.2%), nervousness (20.9%), depression (35.5%), anxiety (30%), tremor (14.5%), and fever (11.8%).

Current Description of AD

Growths and Body Fat

Almost all respondents and medical care providers could palpate growths (95.5%; Fig. 2). Growths were found from scalp (32.4%) and neck (37%) to wrist (33.3%) and distant to metacarpophalangeal joints (28.7%; Fig. 3). The most common location for growths include the leg (95.6%), ventral body (chest, breasts, abdomen, and pelvic area; 88.9%), posterior trunk (82.4%), arms (87%), and buttocks (87%).

FIGURE 1. Histogram of age of presentation of fatty growths in adiposis dolorosa.

FIGURE 2. Three individuals with AD. A1, Forty-two-year-old man, BMI 24.6 kg/m²; A2, growths on the forearm (arrows) of A1; B1, 50-year-old woman with AD, BMI 31.2 kg/m². B2, Isolation of firm subscapular tissue. B3, Isolation of forearm nodules. C1, Subscapular firm folds of a 63-year-old woman (arrows), BMI 48.8 kg/m²; C2, multiple fatty growths on arms from C1; multiple fatty growths on legs from C1.
(70.4%). The ankles (31.5%) and feet had growths (41.7%), including the ventral and plantar foot, metatarsals, and one with growth into the calcaneus. Twenty-four respondents had growths on their face: cheek(s) (79.2%), eyebrow(s) (20.8%), forehead (12.5%), and 1 respondent each had a growth on the chin, nose, or under the eye.

Growthes were variable within individuals, from small firm pea-sized nodules (81.8%) to large but distinct moveable round growths (75.5%) that were soft (79.1%) or firm (75.5%); growths could also be large and indistinct (75.5%). Respondents also described growths that were fixed (55.5%) and deep (70%). Over half of respondents noticed swelling in the area of growths (51.8%); 44% felt skin around the growths wrinkled or puckered.

Many respondents (80.9%) had biopsies, resection, or liposuction of growths from the head (9.1%), mouth (6.1%), neck (13.6%), chest (28.8%), arms (63.4%), abdomen (37.9%), buttocks (24.2%), legs (50%), and feet (9.1%); 23.6% of respondents developed a seroma after surgery. Histologic descriptors from pathology reports included lipomas (54.5%), mature adipose tissue (20.5%), or angiolipomas (40.5%), the latter from the head, neck, chest, arms, abdomen, buttocks, legs, and feet. The

<table>
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<th>Medication/Treatment</th>
<th>Responses</th>
<th>Effect on Pain (%)</th>
<th>Effect on Growths (%)</th>
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<td></td>
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<td>Removal of fat growths</td>
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<tr>
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<td>30</td>
<td>100</td>
<td>0</td>
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<tr>
<td>Religion, spirituality, prayer</td>
<td>28</td>
<td>89.3</td>
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growths had associated fibrous tissue and/or connective tissue capsule (49.4%), were in clusters (43.8%), were yellow (47%) or brown (10%), or looked like yogurt (11.2%).

Respondents estimated the average number of their growths as 112.2 ± 250.8, median 77.3 ± 84.5; 2 individuals counted growths in the 1000s. Because respondents had more growths than at disease onset, we asked respondents to rate the increase in fatty growths over time on a scale of 0–10, with 0 being no change and 10 being very rapid change. Intraindividual growth rates varied from 1 to 10, with an average rate of 6.2 ± 2.4. There was no correlation between number of growths and maximal rate of increase or years of AD. There was a small negative and statistically significant correlation between rate of growth and years of AD (r² = 0.278; P < 0.004), suggesting a more rapid rate of increase in growths early in the syndrome.

The average BMI of respondents was 34.7 ± 8.7 kg/m² (range, 19.2–59.9 kg/m²), and 77.2% of respondents were obese (BMI ≥30 kg/m²).17 Firm, pendulous fat is common in AD.18 (Figs. 2, 3). Respondents had folds of fat on the neck (22.7%), back (36.4%), upper arms (42.7%), inside the knees (39.1%), around the abdomen (61.8%), suprapubically (33.6%), and at the hips (35.5%). Only 17.1% described accumulation of fat on the back of the neck and upper back (buffalo hump). Less than half of respondents felt they could lose weight with exercise and diet (41.8%) and none of the respondents felt they could lose fat from growths.

Of the 110 respondents, 71 (64.5%) had cycles of increased growths and pain. Of these respondents, 49% felt cycle duration was variable from days to weeks, with a range from hours to a year. The majority did not know the cause of cycles, but 21.1% felt it was secondary to stress; 16.9% thought menses, hormonal changes, or estrogen; and fewer thought cycles were secondary to weather change or moon cycles (15.5%), exercise or activity (8.5%), and infection or illness (7%).

Skin (including overgrowths) was tender (74.5%); felt swollen (64.5%); had a burning (61.8%), crawling (51.8%), or pinprick sensation (42.7%); or itched (60.9%). A notable number of respondents described a feeling of hair or fuzz blowing across the skin surface (37.3%) or as if water were running under or on the skin (32.7%).

**Treatment**

All but 1 of the respondents provided a medication list; 4 respondents were on no medications. Pain was treated most commonly with narcotics (43.6%) and nonsteroidal anti-inflammatory drugs (39.6%); also used were topiramate for migraine headaches (8.9%), muscle relaxants (8.9%), tramadol (8%), lidocaine patches or gel (5%), and methadone (2%), and 1 respondent took ketamine. For neuropathic pain, 18.8% took gabapentin or pregabalin, 6% were on tricyclic antidepressants, and 1 individual was administered ziconotide.19

Antidepressants, lidocaine, and visits to a pain control clinic for a variety of treatment all clearly improved pain associated with minimal effect on size or number of growths (Table 2). Corticosteroids improved pain in some but not all, and a greater number felt growths worsened; the number of responses in this group was small. Respondents favored heat over cold for improving pain in the growths, but 32% felt extreme heat worsened pain; fewer respondents felt hot baths worsened pain in growths, suggesting a difference between radiant or weather-related heat and water-based heat. Exercise worsened pain in the majority and worsened growths in 30%. Equivocal responses for pain were found for massage; however, 22% of respondents felt growths worsened. Physical therapy worsened pain in the majority and worsened growths in 35%. Interestingly, a small number of respondents felt chiropractic treatment was beneficial for pain but also felt growths worsened with this treatment. A majority of respondents felt removal of fatty growths improved pain; in a small number of respondents, growths either improved or worsened with liposuction. When we asked specifically about liposuction, 83 respondents (75.5%) reported having had liposuction; of these, 50.6% reported that growths grew back. Imagery, religion, spirituality, and prayer were clearly beneficial for pain in 58 respondents. Alternative treatments were tried by respondents in small numbers: 10 tried acupuncture and 8 felt it helped and 2 felt it worsened pain; 8 tried cannabis and all felt it helped the pain and 1 felt growths improved. One individual reported rHGH improved growths.

**Associated Conditions**

**Cardiovascular**

Many respondents had a rapid heartbeat (78%; frequency, 2.7 ± 1.3); 41% of respondents had a diagnosis of...
cardiac arrhythmia or tachycardia and none had atrial fibrillation. Only 37.6% of respondents complained of a slow forceful heartbeat. A large number of respondents (72%) complained of chest discomfort (frequency, 2.7 ± 1.3). Although risk factors for heart disease were prominent, including obesity (72%), hypertension (41.8%), high total cholesterol (62%), high LDL (14.3%), high triglycerides (56.2%), and tobacco use (15.5%), only 5% of respondents had a history of myocardial infarction and none had a history of stroke. Lipid-lowering medications (statins, fenofibrate, and ezetimibe) were taken by 21%; 51.5% were on antihypertensive medication, including β-blockers and HCTZ, and 21.8% were on ASA or clopidogrel. Only 1.8% had congestive heart failure. Lower-extremity edema was present in 39.1%, and 15.8% were on diuretics, excluding HCTZ. Consistent with obesity, 22.7% of respondents had sleep apnea; of these, 36% were on CPAP. Nine respondents (8.2%) had mitral valve prolapse.

Endocrine

Eighteen respondents (16.4%) had diabetes, 2 age 0–44 years (5.7%), 15 age 45–64 years (21.1%), and 1 between 65 and 74 years (33.4%). The percent of respondents with diabetes by BMI was as follows: 7.6% <25 kg/m², 4.8% from 25.0–29.9 kg/m², 7.1% from 30.0–34.9 kg/m², and 29.2% ≥35 kg/m². Twenty-nine respondents (26.4%) were diagnosed with the metabolic syndrome or insulin resistance or met NCEP guidelines for metabolic syndrome.²⁰ Because birth weight and insulin resistance are associated,²¹ we asked about gestation; prematurity (12.7%) and delayed birth (9.2%) were not prominent, with an average birth weight of (3.4 ± 0.7 kg). Hypoglycemic medications were taken by 70.6% of respondents with diabetes (6, metformin; 6, insulin; 2, sulfonlyureas; 1, exenatide; and 4, thiazolidinediones). Nine individuals with metabolic syndrome were taking metformin (32.1%).

Thyroid disease was prominent (27.3%); 26 had hyperthyroidism or subclinical hypothyroidism (20 were on thyroid replacement), 1 had hyperthyroidism, 1 had multinodular goiter, and 3 had thyroid adenomas. Twenty-two respondents had been tested for growth hormone deficiency; of these, 9 were deficient and 3 respondents were on replacement therapy; an additional respondent with normal insulin-like growth factor-1 levels was also on recombinant human growth hormone. One individual had high insulin levels. One respondent had primary hyperparathyroidism. Hair loss was experienced by 50.9% of respondents, and of these, 85.7% complained of loss of hair on the head.

In women, 16.5% had polycystic ovarian disease; 6% were on bisphosphonates for osteoporosis. Hormones, including hormone replacement therapy or birth control pills, were being taken or had been taken by 49% of the women; only 2 women had increased pain on estrogen and 1 had worsening growths. One woman reported progesterone increased her pain. One woman was on testosterone. When asked about impotence, 17 of 19 men answered and 58.8% of them denied impotence; the remainder had occasional impotence (frequency 2 ± 1.5). Two men (10.5%) had documented low testosterone levels and none were on testosterone replacement.

Since elevated body temperatures were reported in a small number of individuals with AD,⁶ we asked about alterations in body temperature; 16.4% of respondents had a higher body temperature and 34.5% had a lower body temperature than normal.

Gastroenterology

Heartburn was present in 76.8% of respondents; 29.7% were on acid reducers. Almost half of respondents (47.3%) were diagnosed with irritable bowel syndrome (IBS); 82.8% complained of constipation (frequency, 2.8 ± 1.2), 69.5% had loose watery stools about once a month (frequency, 2.4 ± 1.2), and 78.1% complained of nausea monthly (frequency, 2.6 ± 1.2). Five percent were on medication for IBS or constipation, including tegaserod maleate and hyoscymine. Eleven respondents had gastroparesis, but interestingly, only 2 had diabetes. Many respondents (85.9%) complained of bloating after meals >5 times a month. Additional conditions included fatty liver (10.9%), hiatal hernia (3.6%), gastritis (1.8%), and esophageal stricture or dysphagia (1.8%). Five percent took digestive enzymes, laxatives, or Phenergan.

Infectious Disease and Hematology

Almost half (49.1%) of respondents got infections easily since developing AD. Eight of 21 respondents had elevated immunoglobulin G for Epstein-Barr virus, 3 of 12 tested positive for mycoplasma, 4 of 30 tested positive for past Lyme infection, 2 of 38 respondents tested positive for tuberculosis, and 41 respondents tested negative for HIV. Of 67 reporting blood counts, white blood cell counts were normal in 79.1%, elevated in 17.9% high, and low in 3%. Hemoglobin was normal in 80.3%, low in 18.0%, and elevated in 1 man not on testosterone replacement.

Nephrology/Urology

Kidney disease, including proteinuria, nephrolithiasis, and difficulty urinating, was seen in 32.7% of respondents. Urinary incontinence was experienced by 71% at a low frequency (2.8 ± 1.5). Difficulty emptying the bladder was experienced by 42.9% (47% of men) at a low frequency (2.1 ± 1.4), and 39.8% had minimal difficulty starting urination (frequency 1.8 ± 1.2).

Neurologic

The most common neurologic complaints included headache (96%; frequency, 3.4 ± 1.1), which was chronic in 42.7%, dizziness (81.4%; frequency, 2.7 ± 1.3), and blurring or dimming of vision (76%; frequency, 3.0 ± 1.5). Fainting was rare (17.2%; frequency, 1.3 ± 0.7). Another common symptom was numbness in the toes and/or feet (70.5%), fingers and/or hands (57.7%), overgrowths (38%) on arms (24%), legs (42%), buttocks (28%), and face (15%). Respondents also complained of jaw pain (39.1%), loss of balance (40.9%), and sciatica (28.2%). Excess sweating was also common (71.4%; frequency, 3.0 ± 1.5); decreased sweating was reported by only 8.2%. Ten respondents had deafness.
Forty-six respondents had an electromyelogram; of these, 30% had a normal test, 28% had carpal tunnel syndrome, 10.2% had peripheral neuropathy, and the remainder had Guillain-Barré syndrome, dystonia, absent reflexes without diabetes, abnormal somatosensory response, brachial plexopathy, nerve compression secondary to lipomatosis, and demyelination in the hands. Thirty-two respondents had neuropathy; 24 of these also had concomitant depression. The majority of the respondents with neuropathy were on antidepressants (84.4%). A small number of respondents (2%) were on pramipexole for restless leg syndrome.

Psychiatric

Depression was common in respondents (66.4%), with 54% of these on antidepressants. Thirty-three had depression but no neuropathy; 15 were treated with antidepressants. Forty-one of the respondents had depression and neuropathy; 17 were treated with antidepressants.

A large number of the respondents had sleep disturbances (92.7%), including difficulty falling asleep (frequency 3.6 ± 1.4), difficulty staying asleep (frequency 4.0 ± 1.4), frequent awakening during the night (4.2 ± 1.2), and excessive daytime sleepiness (3.8 ± 1.2); 10.9% used sleep aids, including trazodone, and 4% were on clonidine.

Alterations in cognition reported by respondents included difficulty concentrating (66.4%), difficulty expressing thoughts (53.6%), impaired memory (86%; frequency, 3.6 ± 1.4), specifically, short-term (62.7%) and long-term memory loss (20%), and confusion (42.7%; frequency, 2.9 ± 1.4). Anxiety was also prominent (85.4%; frequency, 3.23 ± 1.4), with 14.9% of respondents on benzodiazepines. Additional medications included aripiprazole and lamotrigine for bipolar disease (3%) and modafanil (3%) and phentolamine (1 respondent) for fatigue.

Pulmonary and Allergy

Seventeen respondents had asthma (15.5%), 1 respondent had emphysema, and 1 had restrictive lung disease. Twenty-two people had allergies; a high proportion had various skin sensitivities (41.8%). Very few respondents used an albuterol inhaler (10.9%), but 26.7% were on nonsedating antihistamines or montelukast sodium. Surprisingly, 76.8% of respondents had shortness of breath, with a frequency of 3.0 ± 1.4.

Rheumatologic/Musculoskeletal

Fatigue occurred almost daily (frequency, 4.6 ± 0.9) in a majority of respondents (97%). One respondent had chronic fatigue syndrome and fibromyalgia, and 38.2% had fibromyalgia. Also prominent were joint aches (94%; frequency, 4.2 ± 1.2); 44.5% of respondents had osteoarthritis.

Forty-two individuals (38.2%) had autoimmune disease; 43.9% of these had 2 or more autoimmune diseases. The most prevalent autoimmune diseases were hypothyroidism (22.7%), rheumatoid arthritis (10%), and lupus (4.5%). Other diseases were present in less than 4% of respondents and included adrenal insufficiency, ankylosing spondylitis, celiac disease, Cogan disease, dermatitis, dermatomyositis, Dupuytren contracture, mixed connective tissue disorder, psoriasis, Reynaud disease, scleroderma, Sjögren disease, undifferentiated connective tissue disorder, and vitiligo. Although they did not meet criteria for Sjögren disease, 38.2% complained of dry mouth and 41.8% complained of dry eyes. Medications included methotrexate (2) and hydroxychloroquine (3), 1 was infused tumor necrosis factor (TNF) blocker infliximab, and 1 was weaning off prednisone.

A majority of respondents awoke with muscle pain and stiffness (81.8%). Most reported muscle aches (95.1%) more than 5–7 times a month (frequency, 4.4 ± 1.2), muscle weakness (90.9%; frequency, 4 ± 1.2), and muscle twitching (85.5%), and 72.7% dropped things more often since onset of AD. Of 21 respondents who reported creatine phosphokinase levels, 14.3% had elevated values. A minority complained of a limp (37.3%), atrophy of one (19.1%) or all muscles (18.2%), claw hand (5.5%), or foot drop (7.3%).

Easy bruising was common (74.6%). Just under half (46.4%) had noticeable blood vessels over growths, and 35.5% reported livedo reticularis. Less than half (46.2%) stated phlebotomy was more difficult after developing of AD.

Of 32 respondents, C-reactive protein levels were normal in 66.7% and elevated in 33.4%. Thirty-one respondents were tested for rheumatoid factor (RF); 80.6% were negative and 19.4% were positive. Thirty-two were tested for antinuclear antibodies (ANA); 68.8% had normal tests and 31.2% had positive titers. Thirty-two had erythrocyte sedimentation rates (ESR) evaluated; 67.5% were normal and 37.5% were elevated.

Diet and Exercise

Forty-nine percent of the respondents ate a diet consisting of a mixture of fat and carbohydrates of all kinds, 21% ate a low-fat diet with healthy carbohydrates, 11% ate a low-fat diet with wide variety of carbohydrates, 9.1% were on a diabetic diet, and 3.6% ate a high-fat and -protein diet. Seventeen respondents felt diet affected pain; of these, 58.8% felt it helped pain; 29.4% felt growths improved and 17.6% felt growths worsened.

Only 20.9% of the respondents exercised regularly. A majority (91.8%) reported that AD decreased their desire and ability to exercise; 81% of them stated that their fatty growths hurt more when they exercise.

Habits

Under half of respondents drank alcohol (40.9%), and of these, 4 respondents had more than 1 alcoholic beverage per day on average. Seventeen respondents smoked tobacco (15.5%) and 8 respondents used cannabis.

Family History

Over 45% of respondents reported family members with fatty growths; 49% of family members had painful growths and 62.7% had fewer growths than respondents. The number of affected family members as related to the respondents are as follows: mothers, 14; fathers, 16; daughters, 6; sons, 8; sisters, 14; brothers, 8; maternal grandmothers, 8; maternal grandfathers, 1; paternal grandmothers, 3; paternal grandfathers, 2; maternal aunts, 6; paternal aunts, 3; a niece, 1; maternal cousins, 1; and husbands, 2.
DIscussion

We present results of a survey of 110 men and women with AD. Respondents included Hispanics, African Americans as published previously, and individuals who were part American Indian. Ethnicities of respondents were predominantly Irish, German, or English. There were no Asians among respondents, although reports of AD in Asians exist in the literature. Prevalence and ethnicity in AD would be better achieved through a larger study of defined, populated areas. Although AD is prevalent in Sweden, the majority of respondents to our survey developed AD in the United States. If a 0.1% prevalence rate for AD is correct, then over 300,000 individuals could have AD in the United States. We therefore think AD is a common but poorly identified syndrome.

The age of onset of AD in our respondents was 35 years, consistent with some published data but not others. The ratio of women to men was 5:1, in agreement with previous data.

Fourteen respondents (11.8%), including 42% of the men, had growths and symptoms as children. Although a case of childhood AD has been reported and development of AD suggested in teenagers, the number in our survey was much larger than expected, arguing against AD as a syndrome only of postmenopausal women. In support, the majority of women answering our survey developed AD while menstruating and before age 48 years, less than the average age of menopause expected for this population.

Dercum noted growths in subcutaneous fat in AD, except in the foot; others noted the absence of growths on the face or neck. Our respondents had growths of varying sizes and consistencies in all areas of subcutaneous fat, including the scalp, face, and dorsal foot; the palm was spared. Deep fixed growths in our respondents suggest involvement of deeper tissues such as fascia or muscle. The median number of growths in our study was 75, but respondents had difficulty counting growths. Two individuals estimated growths in the thousands, which could be correct when taking into account the small size and extensive nature of growths.

That the fat in the growths is different from normal adipose tissue is suggested by the inability of any of respondents to lose fat from growths with diet and exercise. Histologically, growths were composed of normal-appearing fat but could also be angiolipomas, and a large number had fibrous tissue. It is possible that the firm folds of fat (Figs. 1, 2) are secondary to increased fibrous tissue. These areas of firmness are also areas in which the subcutaneous fasciae is anchored to deep fasciae or bone, suggesting involvement of connective tissue in growths of AD.

Our survey did not support a hormonal cause of AD. That respondents developed AD as children suggests puberty might play a role. Although menses might exacerbate symptoms, data from our survey were not convincing for menses or pregnancy to play a causal role in AD, as suggested previously. Indeed, 17.6% of the women in our survey were never pregnant. Thyroid disease was also prominent but present in too few individuals to suggest an overall cause. In the ages between 45 and 64 years, the prevalence of diabetes was over twice that of the 2005 US population. Comparing rates of diabetes by BMI, the percent of individuals in our survey with diabetes in the lowest and highest BMI groups was greater than that of published data from NHANES, suggesting that growths in AD might confer insulin resistance even in the absence of obesity.

Many individuals with AD complained of fatigue, weakness, joint aches, muscle pain, and stiffness and had autoimmune disease, suggesting an autoimmune cause for AD; however, laboratory testing of markers for inflammation or autoimmune disease was not confirmatory. A larger study of markers for AD is needed. A majority of respondents had symptoms similar to fibromyalgia such as poor sleep quality and chronic pain, and many respondents were diagnosed with fibromyalgia. Although fibromyalgia and AD coexist, we hypothesize that AD may be misdiagnosed as fibromyalgia. We did not see an increased incidence of Tietze syndrome in respondents, but growths in AD along the sternum and ribs might be mistaken for costochondritis. We also did not find an increased incidence of epilepsy or α-1-antitrypsin deficiency.

Dercum suggested an alteration of “hemolymph” in AD. A leaky lymph system increases fat and infections induce adipose hyperplasia around lymph nodes. Over half of respondents noticed growth-associated swelling, and respondents anecdotally reported changes in size of growths in real time, which could be explained by changes in fluid/lymph. That some respondents had infections and that husbands of affected women also had AD suggests a possible infectious cause.

Since multiple systems are affected in AD, including cardiopulmonary (arrrhythmia, shortness of breath), gastrointestinal (bloating, IBS), psychiatric (depression, sleep disturbances, memory loss), neurologic (neuropathy and hearing loss), rheumatologic (fatigue, muscle weakness, neuropathy), and endocrine (obesity, diabetes), a mitochondrial etiology for AD is intriguing. In mitochondrial disease, paternal transmission would be unlikely but was present in our survey (data not shown) and other publications.

To diagnose AD, other conditions of fatty growths should be considered. Fatty growths should most often appear first on the arm or leg and be accompanied by pain, an unusual presentation for a common lipoma. Onset can be any time from childhood to late adulthood, with a peak in the third decade. Growths should multiply over time and generally be associated with weight gain. Growths should be gently palpated, with deeper palpation of muscles. Pain in growths and joints, fatigue, muscle pain and weakness, and sleep disturbances should be prominent. Failure to lose weight in growths must be present. Other systems should be evaluated for signs and symptoms.

Sleep disturbances should be elicited and neuropsychiatric testing considered. Endocrine testing should include (1) insulin-like growth factor-1 as growth hormone replacement might decrease fat and increase lean mass; (2) testosterone levels in men since low levels are associated with chronic disease and predict mortality and because testosterone replacement increases lean and decreases fat mass; (3) fasting glucose levels or glucose tolerance testing considered. Endocrine testing should include (1) insulin-like growth factor-1 as growth hormone replacement might decrease fat and increase lean mass; (2) testosterone levels in men since low levels are associated with chronic disease and predict mortality and because testosterone replacement increases lean and decreases fat mass; (3) fasting glucose levels or glucose tolerance testing considered; (4) a lipid panel; (5) evaluation for fatty liver and gastroparesis; (6) ECG; (7) pulmonary function tests for shortness of breath; (8) eryth-
rocye sedimentation rate, C-reactive protein, and ANA if treatment is instituted or to evaluate for other disease.

Treatment of AD is symptomatic. Pain is difficult to treat; therefore, a pain specialist should be consulted. Non-steroidal anti-inflammatory drugs, narcotics, antidepressants, agents for neuropathic pain, eutectic mixture of local anesthetics, and topical lidocaine are effective in some. Physical therapy and massage should be avoided unless practitioners are familiar with AD. Visual imagery and warm pool exercise are successful in treating pain. A recent case report suggests infliximab and methotrexate improved AD. Biopsy should be avoided except to rule out other conditions. Surgical resection or liposuction improves pain but recurrence is high. Exercise should be undertaken for overall health but not to decrease growths.

In conclusion, AD is a complex, underdiagnosed, and possibly common syndrome whose hallmark is painful, disabling fatty growths that are unaffected by weight loss. Fatty growths can begin in childhood and progress, ultimately affecting multiple systems. Biopsy does not improve diagnosis, except to rule out other conditions. Treatment is symptomatic, including removal of the fatty growths when pain is unbearable. More research into this interesting focal obesity is needed.

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REFERENCES

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