Sympathetic Joint Effusion in an Urban Hospital

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Objective. Sympathetic joint effusion (SJE) and sympathetic synovial effusion (SSE) are recognized as causes of noninflammatory effusion with <2000 white blood cell (WBC) WBC/mm$^3$ in the joint and bursa, respectively. Data on normal range SJE/SSE with <200 WBC/mm$^3$ are unknown. We aimed to investigate the incidence, disease characteristics, and associated triggers of normal range SJE/SSE and to propose diagnostic criteria.

Methods. This retrospective study included patients hospitalized at Temple University Hospital who underwent a diagnostic arthrocentesis for joint or bursal effusion of unclear etiology from 31 January 2010 to 10 December 2016. A cohort of 72 patients with normal range synovial fluid (<200 WBC/mm$^3$) fulfilled all inclusion criteria for detailed chart review.

Results. Annualized incidence of SJE/SSE was 1.2%. All 72 patients presented with joint pain and swelling. Twenty-three (32%) also had warmth and 12 (17%) had erythema. Symptom onset was hours to within 6 days in 45 (63%) patients. The most commonly affected joint was the knee (61, 85%). Concurrent pathology in close anatomical proximity to SJE/SSE in the same limb was documented in 29 (40%) patients, most of which (26 of 29, 89%) were infection, deep venous thrombosis, intramuscular fluid collection, and trauma. Less common pathology included adjacent recent hip surgery, loosening of hip prosthesis, and extracorporeal membrane oxygenation catheters.

Conclusion. SJE/SSE is not uncommon in hospitalized patients and mimics both inflammatory and septic arthritis. It is seen with normal and noninflammatory synovial fluid. A search for a root cause in the same limb is warranted when evaluating acute or subacute painful joint effusions with normal range synovial fluid WBC count.

INTRODUCTION

Sympathetic joint effusion (SJE), or sympathetic synovial effusion (SSE), is a mimicker of infectious and inflammatory arthritis that contradicts standard clinical correlation. It is a poorly recognized rheumatologic entity that has not been well characterized in the medical literature. Clinically, the patient presents with a painful, swollen joint or bursa with compromised joint function concerning for a septic or inflammatory process. Synovial fluid analysis from this reactive phenomenon, however, reveals a bland, sterile, noninflammatory range of white blood cell (WBC) count (1). SJE is the abnormal formation of a noninflammatory fluid collection in the joint, or SSE if in bursa, in response to primary pathology in an adjacent anatomical structure (1,2).

SJE/SSE has been described in association with infection or inflammation of an adjacent or contiguous anatomic structure (1,2). Early reports described the formation of SJE/SSE adjacent to septic arthritis and septic bursitis (1,2). Others have documented SJE/SSE developing in close proximity to pyomyositis and osteomyelitis, and adjacent to recent orthopedic surgical sites (1–6). In many of these case reports, underrecognition of the SJE/SSE led to misdiagnosis, a delay in the diagnosis, underuse or overuse of antibiotics, and error in treatment duration (1–6).

Noninflammatory range WBC count is defined as less than 2000 WBC/mm$^3$ by synovial fluid analysis. A study with this range of synovial fluid WBC count may be confounded by osteoarthritis (OA), one of the most common rheumatologic disorders. In order to minimize, though by no means eliminate, OA as a confounding cause of effusions, we decided to focus on SJE/SSE with normal range synovial fluid of <200 WBC/mm$^3$. Data on normal range SJE/SSE are completely unknown.
RESULTS

A total of 882 joints were aspirated for synovial fluid analysis over the defined study period of 6.94 years. Eighty joints had preliminary designation of SJE/SSE with normal range (<200 WBC/mm³) joint fluid. Eight joints were excluded for lack of data, positive synovial fluid culture, or for having more than one joint aspirated from the same patient (2, 2, and 4 joints, respectively). A cohort of 72 joints from 72 patients fulfilled inclusion criteria for detailed chart review, resulting in cumulative incidence of 8.2% and annualized incidence of 1.2%. Table 1 shows demographic and clinical characteristics of the 72 hospitalized patients with SJE/SSE. The age range was 18-99 years with a mean age and median age of 60. The majority of the patients were male and African Americans. Onset was from hours to within 6 days in 63% of patients. All patients with SJE/SSE presented with joint pain and joint swelling. Joint warmth was also documented in 32%, and erythema was detected in 17%. The most commonly affected joint was the knee, followed by elbow, shoulder, and hip. Concurrent pathology, either anatomically contiguous or in close proximity to the SJE/SSE in the affected limb, was documented in 40% of patients. No clinical diagnosis of the joint effusion was documented in 71% (51 of 72) of cases prior to and 72% (52 of 72) following diagnostic arthrocentesis. Before diagnostic aspiration, 29% (21 of 72) documented their clinical diagnosis to include septic arthritis (15 of 72, 21%), gout (2 of 72, 3%), SJE (2 of 72, 3%), pseudogout (1 of 72, 1%), overlying cellulitis (1 of 72, 1%), and OA (0%). Subsequent to diagnostic arthrocentesis, only 28% (20 of 72) had a clearly documented final diagnosis. Those final diagnoses included SJE (7 of 72, 10%), OA (5 of 72, 7%), gout (6 of 72, 8%), and pseudogout (2 of 72, 3%), though no crystals were detected, and none thought the etiology of the joint effusion was infectious.

DISCUSSION

Our retrospective study of 72 hospitalized patients is the largest cohort on disease characterization of SJE/SSE to date and the first clinical study dedicated to this topic since 1985 (2). We defined SJE/SSE more stringently for our study by limiting patients to those with normal range joint effusions of <200 WBC/mm³ rather than the noninflammatory range of <2000 WBC/mm³ as reported by previous literature (1–6). This was our attempt to limit OA as a
potential confounding cause of effusions. From the data we gathered, SJE/SSE occurs even in joint effusions classified as "normal range." SJE/SSE is not uncommon, with an annualized incidence of 1.2%. The majority of patients were men with both mean and median age of 60 years. Race was skewed with the majority of patients being African American (Table 1), which represents the

| Variable                           | Descriptor                  | Number Patients | %  |
|------------------------------------|-----------------------------|-----------------|----|
| Age, years                         | Mean 60                     | 72              | 100|
|                                   | Median 60                   | 72              | 100|
|                                   | Range 18-99 (Q1 48, Q3 69)  | 72              | 100|
| Gender                             | Female                      | 26/72           | 36 |
|                                   | Male                        | 46/72           | 64 |
| Race                               | African American            | 38/72           | 53 |
|                                   | Caucasian                   | 16/72           | 22 |
|                                   | Hispanic                    | 10/72           | 14 |
|                                   | Did not self-identify       | 8/72            | 11 |
| Joint symptom                      | Pain                        | 72/72           | 100|
| Joint signs                        | Swelling                    | 72/72           | 100|
|                                   | Warmth                      | 23/72           | 32 |
|                                   | Erythema                    | 12/72           | 17 |
| Symptom Onset                      | Hours, <24                  | 2/72            | 3  |
|                                   | Days, 1-6                   | 43/72           | 60 |
|                                   | Weeks, 1-4                  | 9/72            | 12 |
|                                   | Months, ≥1                  | 2/72            | 3  |
|                                   | No documented onset or duration | 16/72         | 22 |
| Joint affected                     | Knee                        | 61/72           | 85 |
|                                   | Elbow                       | 5/72            | 7  |
|                                   | Shoulder                    | 3/72            | 4  |
|                                   | Hip                         | 3/72            | 4  |
| Concurrent adjacent pathology in same limb | Documented in chart | 29/72 | 40 |
|                                   | None documented             | 43/72           | 60 |
| Diagnosis of joint effusion before synovial fluid analysis | None documented | 52/72 | 71 |
|                                   | Septic arthritis            | 15/72           | 21 |
|                                   | Gout                        | 2/72            | 3  |
|                                   | Sympathetic joint effusion  | 2/72            | 3  |
|                                   | Overlying cellulitis        | 1/72            | 1  |
|                                   | Pseudogout                  | 1/72            | 1  |
| Diagnosis of joint effusion after synovial fluid analysis | None documented | 52/72 | 72 |
|                                   | Sympathetic joint effusion  | 7/72            | 10 |
|                                   | Gout                        | 6/72            | 8  |
|                                   | Osteoarthritis              | 5/72            | 7  |
|                                   | Pseudogout                  | 2/72            | 3  |

Table 1. Demographic and clinical characteristics of 72 hospitalized patients with sympathetic joint effusion
population we serve in North Philadelphia, Pennsylvania, and not a statistical trend by logistic regression (data not shown).

Clinically, SJE/SSE was indistinguishable from inflammatory arthritis or septic arthritis. All 72 hospitalized patients underwent diagnostic arthrocentesis as deemed appropriate by the managing clinicians. All patients had findings of both pain and swelling. Nearly a third also had findings of warmth, and a minority of the patients also had erythema (Table 1). Given signs and symptoms mimicking septic arthritis, acute crystal arthritis, and cellulitis, it was not surprising that anti-inflammatory therapy, corticosteroids, or antibiotics were empirically started in some. Onset of joint symptoms was typically acute, with 63% developing symptoms from hours to within 6 days. No onset or duration of symptoms was documented in 22% of patients. The remaining 15% had symptom onset ranging from a week to months (Table 1). This latter group with subacute to chronic symptomatic effusions may represent OA rather than SJE/SSE. This was suggested by a trend in multiple logistical regression analysis though not statistically significant.

A comparison of the clinical diagnosis of painful joint effusion was made before and after diagnostic arthrocentesis in 72 patients (Table 1). However, 71% of cases had no documented clinical impression or diagnosis before diagnostic aspiration. Review of charts in these instances typically showed the clinicians’ working assessment as “right knee effusion” with plans to check blood tests, perform radiographs of the knee, and perform diagnostic aspiration. Clinicians did document clinical impressions before diagnostic arthrocentesis in 29% of patients and thought they were dealing with septic arthritis, acute gout, pseudogout, or cellulitis, with only 3% of cases where diagnosis of SJE was considered. Empiric treatment with antibiotics or corticosteroids was administered prior to arthrocentesis in some. It is crucial to point out that before diagnostic aspiration, none of the 29 cases with

Table 2. Concurrent adjacent pathology on the same limb of 29 patients with sympathetic joint or sympathetic synovial effusion

| Pathology          | # Patients | % Patients | Type of Pathology (#Pts) | Location of Pathology (#Pts) | Location of SJE/SSE (#Pts) |
|--------------------|------------|------------|--------------------------|------------------------------|----------------------------|
| Infection          | 17/29      | 59         | Cellulitis (6)            | UE (2)                       | Elbow (2)                  |
|                    |            |            | Abscess (5)               | LE (4)                       | Knee (4)                   |
|                    |            |            | Skins near shoulder       | Should (1)                   | Should (1)                 |
|                    |            |            | Shoulder girdle musculature |                             |                            |
|                    |            |            | Antecubital fossa (1)     | Elbow (1)                    | Hip (2)                    |
|                    |            |            | Iliopsoas (2)             | Hip (2)                      |                            |
|                    |            |            | Septic arthritis (1)      | Knee (1)                     |                            |
|                    |            |            | Septic bursitis (1)       | Knee (1)                     |                            |
|                    |            |            | Necrotizing fasciitis (1) | Knee (1)                     |                            |
|                    |            |            | Myofascitis (1)           | Knee (1)                     |                            |
|                    | 3/29       | 10         | DVT (3)                   | RLE (2)                      | Knee (2)                   |
|                    |            |            | Thigh, serous (1)         | BLE (1)                      | Left knee (1)              |
|                    |            |            | Thigh, hematoma (1)       |                             |                            |
| Fluid collection   | 3/29       | 10         | IM fluid collection (3)   | Thick (1)                    | Knee (1)                   |
|                    |            |            |                            | Thigh (1)                    |                             |
| Trauma             | 3/29       | 10         | Crush injury (1)          | Thigh (1)                    | Knee (1)                   |
|                    |            |            | Gunshot wound (1)         | LE (1)                       | Knee (1)                   |
|                    |            |            | Laceration (1)            | LE (1)                       | Knee (1)                   |
| Recent joint surgery | 1/29   | 3.4        | Recent hip surgery (1)    | Hip (1)                      | Knee (1)                   |
| Displaced joint prosthesis | 1/29 | 3.3 | Loosening hip prosthesis (1) | Hip (1)                      | Knee (1)                   |
| ECMO catheters     | 1/29       | 3.3        | ECMO cannulations (1)     | Groin (1)                    | Knee (1)                   |

Abbreviation: BLE, bilateral lower extremity; DVT, deep venous thrombosis; ECMO, extracorporeal membrane oxygenation; IM, intramuscular; L, left; LE, lower extremity; RLE, right lower extremity; SJE, sympathetic joint effusion; SSE, sympathetic synovial effusion; UE, upper extremity.

* Multiple abscesses throughout musculature of shoulder girdle.
Table 3. IJT’s diagnostic criteria for sympathetic joint effusion and sympathetic synovial effusion

| Clinical Features (Fulfil All Four Below): |
|------------------------------------------|
| Monoarticular (1 joint)                  |
| Evidence of joint or bursa inflammation on examination (must have pain and swelling, may also have warmth and/or erythema) |
| Acute onset of joint effusion (hours to <7 days though up to weeks in some) |
| No disorders, such as osteoarthritis, direct trauma to the joint, or fracture that could otherwise explain the joint effusion |

| Synovial Fluid Analysis Features (Fulfil All Three Below): |
|----------------------------------------------------------|
| Normal (<200 WBC/mm³) or noninflammatory (<200 WBC/mm³) range |
| Culture negative for microbial growth |
| No crystals seen |

| Adjacent Pathological Process in Same Limb (Present): |
|------------------------------------------------------|
| Search in the area contiguous, adjacent to, or in close anatomical proximity (both superficial and deep, proximal and distal) to the joint effusion |
| The search is not limited to infection, DVT, intramuscular fluid collection, nearby trauma, recent orthopedic surgery, loosening of joint prosthesis, and ECMO catheter cannulation. Knee SJE/SSE may be seen with foot infection. |

Abbreviation: DVT, deep vein thrombosis; ECMO, extracorporeal membrane oxygenation; SJE, sympathetic joint effusion; SSE, sympathetic synovial effusion; WBC, white blood cell.

Definite SJE/SSE = Clinical features + Synovial fluid features + adjacent pathological process

Probable SJE/SSE = Clinical features + Synovial fluid features

Preliminary diagnosis thought OA was the cause of the painful effusion. Interestingly, even after diagnostic aspiration and synovial fluid analysis, total documentation of final diagnosis increased only by 1%, and the final diagnosis of SJE increased from 3% to 10%. After diagnostic arthrocentesis when synovial fluid was found to be normal without crystals or positive growth in culture, 7% thought they were dealing with effusions from OA, 8% from gout, and 3% thought pseudogout was the culprit. Diagnosis of infection as a cause of the joint effusion decreased from 22% to none following synovial fluid analysis. From the minimal increase in both documented final total diagnosis and final diagnosis of SJE, we speculate that clinicians were baffled by the lack of clinical correlation between clinical exam and synovial fluid results; and they were unfamiliar with this mimic of septic and inflammatory arthritis. Without a clearly documented final diagnosis following diagnostic arthrocentesis, no specific treatment was given for the majority of patients in this cohort. A few had supportive care without significant response, including nonsteroidal anti-inflammatory drugs, topical ice, leg elevation, and off weight bearing. One patient treated with limb immobilization developed worsening symptoms. One patient correctly diagnosed with SJE responded to intra-articular injection with corticosteroids. What we gleaned from our study is that the majority of clinicians do not know what SJE is or were unaware that they were dealing with SJE.

The knee was the most commonly affected joint, though SJE/SSE also affected elbow, shoulder, and hip joints (Table 1). Concurrent adjacent pathology in the same limb as the SJE/SSE was documented in 40% of patients (Table 2). The most commonly associated, or perhaps triggering, conditions of SJE/SSE were nearby infection, DVT, noninfectious fluid collection, or trauma in the same limb. Less common pathology included close anatomical proximity to a recent joint surgery, loosening of joint prosthesis, and ECMO catheters (Table 2). Conversely, 60% of patients had no documented pathology in the affected limb other than the effusion. Lack of documentation may indicate either true absence of abnormal findings, documentation oversight, or examination oversight by clinicians.

The exact etiology and mechanism of SJE/SSE are unknown. Early theories include changes in vascular permeability and localized edema from inflammation or immobilization, imbalance of synovial fluid permeability that is due to disruption of joint fluid turnover and lymphatic system, and joint motion and angle (1,7). Anatomical proximity or the nearest joint appears to play an essential role in the development of SJE/SSE. Though no measurements were taken, closest proximity between pathology and SJE by common sense include prepatellar septic bursitis associated with knee SJE, antecubital fossa abscess associated with elbow SJE, iliopsoas abscess associated with hip SJE, and abscesses of shoulder girdle musculature associated with shoulder SJE. Slightly further between pathology and SJE include leg cellulitis and DVT associated with knee SJE; and thigh hematoma, noninfectious fluid collection, necrotizing fasciitis, and crush injury associated with knee SJE. Some pathology in or near hip joint have predilection for the knee. Septic arthritis of hip, recent hip surgery, displaced hip prosthesis, and ECMO catheter cannulation in the groin were associated with knee SJE (Table 2). Proximity to or being the nearest joint to pathology is not the sole determinant of SJE location. Interestingly, two patients with foot osteomyelitis developed ipsilateral SJE of knee and not the ankle (Table 2). We also know that in the same individual, similar joints did not consistently develop SJE despite having the same underlying pathology. One patient with bilateral DVT developed SJE in his left knee but not in his right knee (Table 2). The underlying mechanism in the development of SJE/SSE is multifactorial but remains to be unraveled.

Herein, we propose an updated definition of SJE/SSE to include normal synovial fluid to the historically noninflammatory synovial fluid. We define SJE/SSE as an acute formation of a normal or noninflammatory fluid collection in the joint or bursa in response to primary pathology in the adjacent anatomical structure.

Senior author, Irene J. Tan, proposed diagnostic criteria for SJE/SSE (Table 3). SJE/SSE is definite when three features are
fulfilled and probable when the first two of the three features are fulfilled. The three features for consideration are clinical, synovial fluid analysis, and findings of an adjacent pathological process in the same limb as the joint effusion. The clinical features must fulfill four variables: the patient should have only one symptomatic joint (monoarticular); evidence of joint or bursal inflammation (which must have pain and swelling, though warmth and/or erythema may also be seen); acute onset of joint effusion from hours to 6 days (though up to weeks in some); and no active disorders, such as OA, direct trauma to the joint, or joint fracture that could otherwise explain the joint effusion. The second feature is having a normal to noninflammatory synovial fluid by analysis, ie, <200 WBC/mm3 and <2000 WBC/mm3, respectively, with absence of crystals and no microbial growth on synovial fluid culture. The last feature is the presence of an adjacent pathological process. The onus is on the clinician to perform a systematic search for triggering or concurrent pathology in ipsilateral limb affected by joint effusion. The pathological process may be found contiguous, adjacent to, or in close anatomical proximity to the joint effusion. A search for pathology should not be limited to infection, DVT, intramuscular fluid collection, nearby trauma, evidence of recent orthopedic surgery, displaced joint prosthesis, and ECMO catheter cannulation. Knee SJE/SSE may be seen with infections of the foot.

We believe our study will improve recognition of SJE/SSE as a mimicker of septic and inflammatory arthritis with a paradoxically normal to noninflammatory range synovial fluid WBC count. A search for underlying pathology in the same limb, such as adjacent infection, DVT, intramuscular fluid collection, trauma, and complications of orthopaedic surgery, is warranted. We updated the definition of SJE/SSE. Author Irene J. Tan proposed diagnostic criteria for SJE/SSE with the hope of increasing recognition and diagnosis of this reactive phenomenon.

ACKNOWLEDGMENTS

The authors thank the patients in the study; Daohai Yu, PhD, for statistical analysis; and Mark Weiner, MD, for generating the patient list.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content. All authors approved the final version to be submitted for publication. All authors had full access to all data in the study and take responsibility for the integrity of the data and accuracy of data analysis.

Study concept and design. Tan.
Acquisition of data. Barlow.
Analysis and interpretation of data. Tan, Barlow.

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