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A PROSPECTIVE STUDY OF THE SAFETY OF JOINT AND SOFT TISSUE ASPIRATIONS AND INJECTIONS IN PATIENTS TAKING WARFARIN SODIUM

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Objective. **To determine the safety of joint or soft tissue aspirations and injections in patients taking warfarin sodium.**

Methods. **The outcome of 32 joint or soft tissue aspirations or injections in patients receiving stable doses of warfarin sodium was assessed through a standardized interview 4 weeks after the procedure. The primary outcome measure was significant joint or soft tissue hemorrhage, ascertained by patient-reported increases in swelling or warmth at the procedure site.**

Results. **None of 32 procedures was complicated by joint or soft tissue hemorrhage reported by the patients, yielding, by the "rule of threes," a risk of significant hemorrhage of <10% (with 95% certainty). Diagnostic information was obtained for 53% of aspirated sites (8 of 15) and therapeutic benefit was noted in 74% of corticosteroid-injected sites (17 of 23).**

Conclusion. **Joint or soft tissue injections and aspirations in selected patients taking warfarin sodium are associated with a low risk of hemorrhage and are often of diagnostic or therapeutic value.**

The clinician faces a dilemma when considering joint or soft tissue aspirations or injections in patients who are taking warfarin sodium (Coumadin; DuPont, Wilmington, DE). The potential benefits of these procedures are often overshadowed by the specter of iatrogenic hemarthrosis or soft tissue hemorrhage. Although case reports from the era before the introduction of the International Normalized Ratio (INR) document the occurrence of spontaneous hemarthrosis (1,2) and joint destruction (3) in patients receiving warfarin sodium, the risk of hemorrhage following joint or soft tissue procedures in patients taking therapeutic doses of warfarin sodium is unclear. We hypothesized that joint and soft tissue aspirations or injections could safely be performed in patients taking therapeutic doses of warfarin sodium, and we conducted a prospective cohort study to assess the safety of such procedures in these patients.

PATIENTS AND METHODS

Patients. From October 1996 to mid-July 1997, patients who were taking warfarin sodium and who had joint or soft tissue aspirations or injections performed by the rheumatology service at the Rheumatology Procedure Clinic or affiliated hospitals at our institution were identified at the time of the procedure. Inclusion criteria for this study were the use of a stable dose of warfarin sodium and a most recent INR value of <4.5. Exclusion criteria were an INR value of >4.5, concomitant use of heparin, or the presence of overlying cellulitis.

Thirty-two procedures were performed in 25 subjects during this period. All subjects fulfilled the inclusion criteria and agreed to participate in this study. Study approval was granted by the Institutional Review Board.

Aspirations and injections. Aspirations and injections of joints and soft tissues using standard techniques were performed under aseptic conditions by a staff rheumatologist or by a rheumatology fellow or internal medicine resident under the supervision of a staff rheumatologist. Informed consent was obtained from all subjects.

The needle size typically used was 18F for knee aspirations, 20F for other procedures, and 25F for aspiration or injection of the first metatarsophalangeal (MTP) joint. Betamethasone (Celestone; Schering, Kenilworth, NJ) or methylprednisolone (Depo-Medrol; Pharmacia and Upjohn Co., Kalamazoo, MI) was used for corticosteroid injections. A subcutaneous local anesthetic (1% lidocaine) was typically given prior to aspirations but not injections. Patients were instructed to avoid strenuous activities and excessive movement of the injected/aspirated site for 24–48 hours after the procedure.

Assessment. The main outcome measure was significant joint or soft tissue hemorrhage, ascertained by patient-

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Table 1. Thirty-two joint and soft tissue aspirations and injections in 25 patients receiving warfarin sodium*

Site (no. of procedures)	International normalized ratio			Underlying rheumatic disease (n)
	Aspiration	Injection	Aspiration and injection	
Joints (15)				
Wrist (2)	2.2, 3.1†	–	–	Gout (1), pseudogout (1)
Elbow (1)	3.1†	–	–	Gout (1)
Knee (8)	1.8, 3.7‡	2.2, 2.3	2.7, 3.1†, 3.1, 3.4	OA (2), pseudogout (2), inflammatory arthritis (2)
Ankle (2)	3.0‡	–	2.2‡	Gout (1)
First MTP (2)	3.9	–	1.8‡	Gout (2)
Soft tissues (17)				
Olecranon bursa (2)	2.2, 3.1†	–	–	RA (1), gout (1)
Subacromial bursa (4)	–	1.5, 2.5, 2.6, 4.3	–	RA (1), APS (1)
Biceps tendon (2)	–	2.6†, 2.8‡	–	RA (1)
Greater trochanteric bursa (6)	–	1.7, 1.7, 1.8, 2.3, 2.7, 2.7	–	None
Pes anserinus bursa (3)	–	1.6, 1.7†, 2.9‡	–	None

* Corticosteroids were instilled in all injections (23 of 23), and 1% lidocaine in 95.6% of injections (22 of 23). OA = osteoarthritis; MTP = metatarsophalangeal; RA = rheumatoid arthritis; APS = antiphospholipid antibody syndrome.
† Patient taking nonsteroidal antiinflammatory drugs or low-dose aspirin.
‡ Thrombocytopenia.

reported increases in swelling or warmth at the procedure site. A standardized telephone interview conducted by either author was used to obtain followup information on the development of increased warmth, swelling, or bruising at the procedure site, and any treatment received for procedure-related complications. A 4-week interval between the procedure and the assessment was chosen so that information on treatment for hemarthroses would be available.

Patients who were given corticosteroid injections were asked to rate pain in the injected site at the time of the interview as worse, slightly better, much better, or resolved. Patient contact was initiated 4 weeks after the procedure and was successful a median of 5.0 weeks (range 4.0–11.6 weeks) after the procedure. There were 2 exceptions to this. In 1 patient who had a wrist aspiration and inconsistent symptom reporting due to early dementia, outcome was based on assessment by a staff rheumatologist (not involved in this study) 3 days after the procedure. In another patient who underwent 2 ankle procedures 3 weeks apart while hospitalized, outcome was based on patient self-report 2 weeks after the first procedure. Chart abstraction of demographic and other data was performed by 1 physician abstractor (JT) using a standardized, pretested data collection form.

RESULTS

Thirty-two joint or soft tissue aspirations or injections (see Table 1) were performed in 15 male and 10 female patients who had a median age of 74 years (range 45–87 years). INR assays were performed a median of 1.5 days (range 0–129 days) prior to the procedure. The median INR value was 2.6 (range 1.5–4.3). In only 1 instance (an injection of the pes anserinus bursa) was the INR study done more than 1 month prior to the procedure; that patient was taking a stable dose of warfarin sodium and had INR values ranging from 2.0 to 3.0.

The reasons for anticoagulation therapy in this patient series included cerebrovascular disease, atrial fibrillation, other cardiac disorders, and lower extremity deep vein thrombosis. Seven procedures were performed in subjects taking nonsteroidal antiinflammatory drugs or low-dose aspirin, and 5 procedures in subjects with thrombocytopenia (platelet counts ranging from 96 to 129 $\times$ 10^9/liter; normal $>150 \times 10^9$/liter). In 95.6% of injections (22 of 23), 1% lidocaine was instilled, with a median dose of 2 ml (range 0.3–5.0 ml).

None of the 32 procedures was associated with patient-reported joint or soft tissue hemorrhage. The risk of significant joint or soft tissue hemorrhage by patient self-report in this series was therefore $<10\%$ (with 95% certainty) by the "rule of threes," which states that if no events of a particular type occur in a study of x individuals, then one can be 95% certain that the event of interest occurs no more often than $3/x$ (4). The "rule of threes" quantifies the risk of clinically significant joint or soft tissue hemorrhage, taking into account the number of procedures in this study.

Diagnostic information was obtained for 53% of aspirated sites (8 of 15): crystal-induced arthritis was confirmed in 7 instances, and septic olecranon bursitis was excluded in 1 instance. Resolution or marked improvement of pain occurred in 74% of corticosteroid-injected sites (17 of 23). Small amounts (0.1–0.5 ml) of bloody fluid were noted in 1 ankle aspiration and 2 aspirations-cum-injections (ankle, first MTP joint) performed over 1 month in a patient with refractory polyarticular gout. These were thought not to represent

significant hemarthroses, since aspirates from these sites are often bloody, and clinical assessment of the procedure site by a rheumatologist or physician shortly after each procedure did not reveal features of a hemarthrosis.

DISCUSSION

This prospective cohort study suggests that joint and soft tissue aspirations and injections in patients taking therapeutic doses of warfarin sodium are associated with a low risk of hemorrhage and are often of diagnostic or therapeutic value. The risk of clinically significant joint or soft tissue hemorrhage in this series was <10%, while diagnostic information was obtained for 53% of aspirated sites and therapeutic benefit was noted in 74% of corticosteroid-injected sites. With the increasing use of long-term anticoagulation therapy in patients with nonvalvular atrial fibrillation (5) and other disorders, rheumatologists may occasionally encounter a patient receiving warfarin sodium in whom joint or soft tissue aspiration or injection would be beneficial. This study provides information on the risks and benefits in such a situation. Of note, our data are consistent with studies suggesting the safety of intramuscular (6) and other (7) injections in such patients.

Our data do not imply that joint or soft tissue aspirations or injections are safe in all patients taking warfarin sodium. Although the risk of significant joint or soft tissue hemorrhage is relatively low, it is likely to be higher than the risk in patients not receiving warfarin sodium and may be further increased in the presence of underlying joint disease (1), thrombocytopenia, or use of antiplatelet agents or heparin (8). The intensity of anticoagulation, the presence of comorbidities (9), and the injection or aspiration technique may also influence the risk of hemorrhage. The decision to perform such procedures in a patient taking warfarin sodium should therefore be individualized. Corticosteroid injections should only be considered if symptoms are disabling and conservative measures have failed. Although lidocaine is a vasodilator which could theoretically predispose to injection-site bleeding, it is the preferred local anesthetic in our procedure unit because it rarely causes allergic reactions.

We cannot exclude the possibility that joint aspiration or injection in patients taking warfarin sodium may cause subclinical hemarthrosis. Repeated subclinical hemarthroses may contribute to the arthropathy seen in patients with hemophilia (10). It is unclear if a similar process occurs in patients taking warfarin who develop postprocedural subclinical hemarthrosis. Nevertheless, the benefits of joint aspirations or injections in these patients are likely to outweigh this potential risk because of the significant morbidity associated with misdiagnosing or incorrectly treating arthritis and the beneficial effects of corticosteroids on hemarthrosis-related synovial inflammation (11).

We recognize several limitations of this study. The assessment of joint or soft tissue hemorrhage was based on self report because of the impracticality of having all patients return for clinical evaluation, and the cost of pre- and postprocedure magnetic resonance imaging. Because significant joint or soft tissue hemorrhages are typically symptomatic, it is unlikely that patients would have failed to notice their occurrence. It is possible that after a 5-week interval, the patients might not recall the symptoms associated with a hemarthrosis. This seems unlikely, given the usually prominent nature of these symptoms. Because the number of subjects studied was not large, we did not determine the risk of hemorrhage at individual sites or in the presence of other factors that predispose to bleeding.

In conclusion, our data suggest that diagnostic joint or soft tissue aspirations may be successful and without complications if carefully performed in selected patients taking warfarin sodium. Therapeutic joint or soft tissue injections are not contraindicated in such patients, provided that there is not excessive anticoagulation (INR >4.5), the influence of other factors predisposing to hemorrhage is minimal, and conservative measures have failed.

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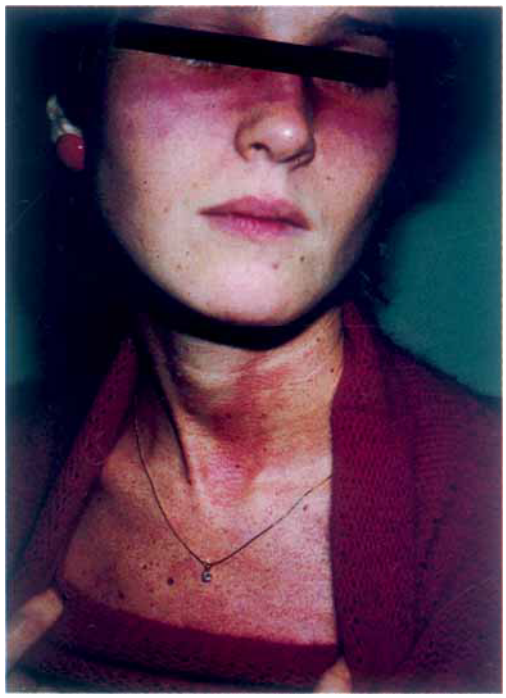
Clinical image: Severe neuropsychiatric lupus responding to long-term, intermittent plasmapheresis



The patient is a 35-year-old woman with severe neuropsychiatric lupus (further described in Neuwelt CM, Asherson RA, Daikh DI. Reply to letter to the editor by Golden and Belmont [letter]. Arthritis Rheum 1998;41:753–754.) spanning 18 years, with a vaso-occlusive retinopathy and intermittent severe organic brain syndrome representing lupus cerebritis with psychosis, visual and auditory hallucinations, and seizures. The intense malar rash and cutaneous vasculitis seen here correlate quite well with her flares of lupus cerebritis. Because of her diffuse presentation, she has undergone brain magnetic imaging studies and laboratory evaluations for antiphospholipid antibody syndrome, and the results have been negative. As stated elsewhere (Reply to letter to the editor by Golden and Belmont), it is postulated that her unique and unusual response to corticosteroids and long-term, intermittent plasmapheresis therapy represents a reversal of leukoagglutination, perhaps through the removal of cytokines or other mediators that disrupt the activation of vascular endothelium.

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