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The effectiveness of computed tomography-guided biopsy for the diagnosis of spondylodiscitis: an analysis of variables affecting the outcome

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Abstract. – OBJECTIVE: To analyze: (i) the effectiveness of CT-guided biopsy for the diagnosis of suspected spinal infections (spondylodiscitis); (ii) identify common causative microorganisms and assess factors that could affect the diagnostic yield.

PATIENTS AND METHODS: Forty-five patients undergoing CT-guided biopsy for suspected spinal infection between November 2012 and October 2014 were analyzed. The time from presentation to diagnosis, administration of antibiotics before biopsy, blood culture results, admission C-reactive protein (CRP)/white cell count, presence of fever or neurological deficits, and soft tissue collections on MRI were analyzed. Multivariable logistic regression was performed to determine variables independently associated with a positive biopsy.

RESULTS: Eleven (24.4%) patients had positive blood cultures. The first biopsy was positive in 19 (42.2%) patients. Thirty-eight (84.4%) patients had a single biopsy, while seven (15.5%) patients underwent repeat biopsy with a positive yield in one (14.2%) patient. Overall, causative microorganisms were identified in 26 (57.8%) cases. Admission CRP was significantly associated with isolating the causative pathogen from CT-guided biopsy ($p<0.001$). A soft tissue collection on MRI was associated with identification of a microorganism in blood cultures ($p=0.001$). CRP was the only independent variable associated with a positive yield on CT-guided biopsy ($p=0.007$, OR 1.042) and was more likely in patients with CRP>50 ($p<0.001$). Administration of empirical antibiotics before biopsy did not affect the yield ($p=0.572$).

CONCLUSIONS: A high CRP was a strong predictor of isolation of the causative organism. Repeat CT-guided biopsy was found to have limited value with a low positive yield (14.2%) in our study.

Key Words:
Discitis, Spondylodiscitis, Spinal infection, CT-guided biopsy.

Introduction

Spondylodiscitis is an infection of the intervertebral disc and adjacent vertebrae that occur more commonly in patients aged over 50 years[1]. Diagnosis can be delayed by two to six months[2-4] due to insidious symptom onset, predominantly back or neck pain. Neurological deficits have been reported in about one-third of patients[4,5]. Between 10% and 45% of patients are febrile at presentation[3,6]. The majority of patients with spondylodiscitis can be treated medically with antibiotics based on organism sensitivity as identified in blood or tissue biopsy cultures[7-9]. Surgery is usually indicated in patients with neurological compromise, mechanical instability, or failed conservative treatment[2,10-12]. Suspected spondylodiscitis requires further workup, in which computed tomography (CT)-guided needle biopsy plays a crucial role[13-15]. There is wide variability in the literature on the sensitivity of CT-guided biopsy for the identification of the causative organism, ranging from as low as 19% to as high as 90%[5,6,14,16-22]. In some studies[4,23] blood cultures are reported to be positive in 50% to 72% of patients. However, blood culture isolates do not always correlate with culture results from needle biopsy; therefore, a needle biopsy may be warranted in cases in which an alternative source of bacteremia is suspected[23]. Patients with negative Gram stains and culture results should begin empirical antimicrobial therapy directed at the more common microorganisms known to cause spondylodiscitis. Only a limited number of investigations have evaluated the need and efficacy of repeat CT-guided biopsy in patients with a negative blood culture and negative first CT-guided biopsy. Therefore, we assessed the efficacy of CT-guided biopsy for the diagnosis of suspected spinal infections and included patients that had begun receiving empiri-

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cal antibiotic treatment. Additionally, we analyzed the effectiveness of repeat CT-guided biopsy and its effect on the final diagnostic yield. We gathered data on microbiology patterns to guide empirical treatment in our patients with a negative blood culture and negative CT-guided biopsy. Factors that could independently improve diagnostic yield were also analyzed.

Patients and Methods

This was a retrospective observational study, in which data were collected from medical charts. We employed the UK NHS Health Research Authority Tool (http://www.hra-decisiontools.org.uk/research/), which deemed this work to be service evaluation and no further Ethics Approval or consent was required. Patients were eligible for the study if they had a suspected spinal infection based on clinical and magnetic resonance imaging (MRI) findings and underwent CT-guided biopsy at our institution between November 2012 and October 2014. Forty-five patients met these inclusion criteria. Patients were identified in the records using radiology codes and were cross-referenced with the hospital's neurosurgical database. Patients with postoperative spinal infections were excluded. Data were collected retrospectively from the case notes and microbiology records of the forty-five eligible patients. Data collected were: spinal discitis, time from presentation to diagnosis, number of attempts at CT-guided biopsy, administration of antibiotics within two weeks of biopsy, blood culture results, admission C-reactive protein (CRP), admission white cell count (WCC), the presence of fever, neurological status, and presence of a soft tissue collection on MRI. The normal laboratory ranges for WCC and CRP were 4.00–11.00 $\times$ 10^9 cells/L and <10 mg/L, respectively. Percutaneous CT-guided biopsies were performed in the imaging department by a radiologist. Microbiology results from the biopsy specimens were collated to identify the isolated pathogens.

Statistical Analysis

Baseline characteristics between the two groups (with or without a positive yield on CT-guided biopsy) were compared using the Student's *t*-test for parametric variables and the Mann-Whitney test for non-parametric variables. Categorical data were analyzed using the χ^2 test. A cut-off value for CRP was chosen from the coordinates of the ROC curve that maximize both sensitivity and specificity for a positive first biopsy. Multivariable logistic regression was used to determine variables independently associated with a positive yield on CT-guided biopsy. Statistical analyses were performed with IBM SPSS v22 (IBM Corp, Armonk, NY, USA). The significance level was set at $p<0.05$.

Results

The 45 patients included in this study had a mean age of 62.31 (range, 28-87) years at the time of presentation. The median duration of symptoms before presentation was 38 days (IQR, 24-60) (Table I). The spinal infection was cervical in three (6.7%), thoracic in 11 (24.4%), thoracolumbar in six (13.3%), and lumbar in 25 (55.6%) cases. Six (13.3%) patients were febrile at presentation, and nine (20%) had some form of neurological deficit at onset. Four patients had motor weakness and a sensory deficit, two patients had isolated motor weakness, only two patients had sensory symptoms, and one patient had isolated bladder dysfunction. In addition to the findings of spondylodiscitis, MRI scans showed a soft tissue collection in 12 (26.6%) patients. Three patients had epidural abscesses, five patients had paravertebral collections, two patients had combined epidural and paravertebral collections, and two patients had psoas abscesses. Overall, causative pathogens were identified in 26 (57.8%) cases. Eleven (24.4%) patients had positive blood cultures. The presence of a soft tissue collection on MRI was associated with identification of microorganisms on blood cultures ($p=0.001$). The first CT-guided percutaneous needle biopsy identified the microorganism in 19 (42.2%) patients. The most frequently identified organism was *Staphylococcus aureus*, which was isolated in seven (26.9%) patients, one being methicillin-resistant. The next most commonly identified microorganisms in the first biopsy were *Escherichia coli* (11.5%) and coagulase-negative staphylococci (11.5%). A second CT-guided biopsy was performed in seven (15.5%) patients with initial negative blood culture and a negative first biopsy. A second CT-guided biopsy had a positive yield in only one (14.2%) patient who had *Spondylodiscitis* at L5/S1. In that case, *Staphylococcus epidermidis* and *Propionibacterium acnes* were isolated (Table II). Ten (22.2%) patients had already begun empirical antibiotic treatment in the two weeks before the

Table I. Baseline characteristics of the patients.

Variable	Organism isolated on first CT-guided biopsy N = 19	No organism isolated on first CT-guided biopsy N = 26	*p*-value
Age, years, mean (range)	62.73 (32-87)	62 (28-86)	0.877*
Sex, male/female ratio	12/7	14/12	0.532**
Duration of symptoms before presentation, days, median (IQR)	35 (21-45)	43.5 (24-82)	0.173***
Admission C-reactive protein (mg/L), median (IQR)	82 (64-102)	38 (22-68)	<0.001***
C-reactive protein >50, n (%)	16 (84.2)	8 (30.7)	<0.001**
White cell count (×109)	8.22 (3.5-15.4)	8.65 (2.4-19)	0.666*
Level of infection (single/multiple)	13/6	23/3	0.097**
Soft tissue collection, n (%)	5 (26.3)	7 (26.9)	0.964**
Neurological deficit on admission	6 (31.6)	3 (11.5)	0.097**
Empirical antibiotics prior to CT-guided biopsy, n (%)	5 (26.3)	5 (19.2)	0.572**
Febrile on admission, n (%)	4 (21.1)	2 (7.7)	0.193**
Organism identified on blood culture, n (%)	5 (26.3)	6 (23.1)	0.803**

IQR = interquartile range; *Student's *t*-test; **χ2 test; ***Mann-Whitney Test.

Table II. Pathogens identified in patients with positive first biopsy or positive blood culture (N = 25).

CRP[a] (mg/L)	Blood culture result	First biopsy result	On empirical antibiotic
165	*Staphylococcus aureus*	*Staphylococcus aureus*, *Propionibacterium acnes*	Yes
25	MRSA	MRSA	Yes
98	*Staphylococcus aureus*	*Propionibacterium acnes*[b]	No
80	*Staphylococcus aureus*	Negative	No
135	Coagulase-negative *Staphylococcus*	Negative	No
129	*Pseudomonas aeruginosa*	*Pseudomonas aeruginosa*	Yes
30	*Staphylococcus epidermidis*	Negative	No
26	*Staphylococcus aureus*	Negative	No
52	*E. Coli*	Negative	No
90	*Streptococcus agalactiae* sp.	Negative	No
80	*Micrococcus* sp.d	*Staphylococcus capitis*[c]	No
125	Negative	*Staphylococcus aureus*	No
68	Negative	*Staphylococcus aureus*	Yes
130	Negative	*Escherichia Coli*	No
70	Negative	*Escherichia Coli*	No
58	Negative	*Coagulase-negative Staphylococci*	No
30	Negative	*Coagulase-negative Staphylococci, Propionibacterium acnes, Streptococcus mutans*	No
93	Negative	*Enterococcus faecium*	Yes
87	Negative	*Group B haemolytic Streptococci*	No
70	Negative	*Klebsiella oxytoca*	No
38	Negative	*Mycobacterium tuberculosis*	No
102	Negative	*Non-haemolytic Streptococci, Propionibacterium sp.*[b]	No
82	Negative	*Propionibacterium acnes*	No
64	Negative	*Candida albicans*	No
100	Negative	*Streptococcus sanguis*	No

[a]on admission, [b]enrichment culture, [c]uncertain significance, [d]probable contaminant.

CT-guided biopsy. Administration of antibiotics did not show any statistically significant impact on bacterial growth following biopsy in our study (p=0.572; Table I). The median CRP on presentation was 58 mg/L (IQR, 30-90). Admission CRP was significantly associated with the possibility

Table III. Multivariate analysis of factors affecting the outcome of first CT-guided biopsy.

Predictor	N = 45	*p*-value	OR
Age, years, mean (range)	62.31 (28-87)	0.175	0.961
Sex, male/female ratio	26/19	0.292	2.871
Duration of symptoms before presentation, days, median (IQR)	38 (24-60)	0.204	0.988
C-reactive protein (mg/L), median (IQR)	58 (30-90)	0.007	1.042
White cell count (× 109), mean (range)	8.46 (2.4-9)	0.143	0.827
Level of infection (single/multiple)	36/9	0.094	8.450
Empirical antibiotics prior to CT-guided biopsy, n (%)	10 (22.2)	0.833	0.801
Soft tissue collection, n (%)	12 (26.7)	0.159	0.177
Positive blood culture, n (%)	11 (24.4)	0.586	1.864
Febrile on presentation, n (%)	6 (13.3)	0.894	0.832
Neurological deficit, n (%)	9 (20)	0.150	4.177

OR: odds ratio

of isolating the causative pathogen from CT-guided biopsy ($p<0.001$). A CRP > 50 on admission were predictive of isolating a causative pathogen from first CT-guided biopsy with a sensitivity of 84.2% and specificity of 73.1%. In logistic regression, admission CRP was the only independent variable that predicted a positive yield from the CT-guided biopsy ($p=0.007$, OR 1.042; Table III). In conclusion, a high CRP is a strong predictor of causative organism isolation, and a positive biopsy yield is more likely in patients with CRP > 50 ($p<0.001$) and in patients with associated soft tissue collection on MRI. Careful consideration must be given to cases with a negative culture result. Repeat CT-guided biopsy can be considered in non-responsive patients or those with suspected polymicrobial infections, although the positive yield in our study was low (14.2%). A provisional recommendation for antimicrobial therapy can be based on frequently identified organisms, namely *Staphylococcus spp.*

Discussion

Percutaneous CT-guided needle biopsy is the mainstay of diagnosis of spinal lesions, and its safety and efficacy are reported in various studies[6,16,24]. Here we report a positive culture rate of first CT-guided spinal biopsy of 42.2% in patients with symptoms and MRI findings suggestive of infection. We wanted to evaluate the usefulness of repeat CT-guided biopsy in cases where a primary biopsy and blood culture were non-diagnostic. In our study, blood cultures identified the causative organism in 11 (24.4%) patients, and the first CT-guided biopsy isolated an organism in another 14 patients that had a negative blood culture, increasing the number of patients with a microbiological diagnosis to 25 (55.5%). Performing a second CT-guided biopsy in seven patients with a negative first biopsies or blood cultures only identified a microorganism in one patient. Therefore, the causative microorganism was identified in 26 (57.8%) patients overall. In contrast, in a retrospective study by Gras et al[19], the yield from first percutaneous needle biopsy (PNB) was 43.4% (59/136) and 39.4% (13/33) from the second PNB in 33 patients following an initial negative biopsy. In their series, a second PNB (after an initial negative biopsy) led to a microbiological diagnosis in nearly 80% of patients. The high diagnostic yield of second PNB in their study could be explained by the fact that a significant number of the patients (63.9%) had a previous history of spinal surgery, and 43.1% of those had surgical site infections that occurred within 1 year of surgery. We only included patients with primary hematogenous spondylodiscitis and excluded patients with postoperative spinal infection. Of the various routine laboratory tests, C-reactive protein (CRP) is a useful biomarker that is increased in over 80% of patients with spondylodiscitis[25,26]. In our study, the median CRP on presentation was 58 mg/L. By logistic regression, a high CRP was found to be a strong predictor of isolation of the causative organism. Torrie et al[27] performed a retrospective study on 96 patients with spinal infection and reported a significant positive correlation of both admission CRP ($p=0.031$) and WCC levels ($p=0.056$) with a positive isolation of the causative microorganism in either blood or biopsy cultures. In their study, univariate analysis showed that the duration of preceding symptoms was negatively correlated with the chances of isolating a causative organism[27]. In contrast, our study failed

to show any significant correlation between the admission WCC levels or the duration of preceding symptoms and the chance of isolating a causative organism. The microbiologic analysis of the CT-guided biopsy was positive in 26 of 45 cases (57.8%). *Staphylococcus aureus* was the most commonly isolated organism in our study (7/26 cases, 26.9%). This finding is in agreement with most of the reported literature, with *S. aureus* accounting for 30% to 80% of the isolated organisms[2,28-31]. Fantoni et al[29] conducted an epidemiological study and found Gram-negative bacilli as causative agents in 7% to 33% of patients and coagulase-negative *Staphylococci* in 5-16% of patients with pyogenic Spondylodiscitis. The impact of empirical antibiotic therapy on the microbiological yield from biopsy has been evaluated in various studies. In a retrospective study, Kim et al[32] found that antibiotic exposure before microbiologic diagnosis, especially of four or more days, was strongly associated with negative cultures ($p<0.001$). De Lucas et al[21] observed a significantly lower diagnostic yield of CT-guided fine needle aspiration biopsy in patients with previous antibiotic treatment (23% vs. 60%, $p = 0.013$). However, another study failed to show any negative impact on pathogen recovery following biopsy in cases with antibiotic exposure within 14 days of biopsy[33]. In the present study, administration of antibiotics did not have any significant impact on the bacterial growth following biopsy ($p=0.572$), which seems to support the results of the latter study. Recently, other inflammatory markers such as serum procalcitonin (PCT) are being increasingly used for diagnosis of bacterial infection and to monitor treatment response[34]. A systematic review and meta-analysis[35] have shown that the PCT level was more sensitive and more specific than CRP levels for differentiating bacterial from non-infective causes of inflammation. In comparison to CRP, serum PCT was found to be a more reliable marker for predicting early postoperative infection in patients with acute traumatic spinal cord injury[36]. The usefulness of PCT in diagnosing spondylodiscitis has not been established. Maus et al[37] did not find PCT as a useful diagnostic tool or monitoring parameter for spondylodiscitis. In their study, the PCT level was not elevated in a group of 17 patients with spondylodiscitis in comparison to a control group of 18 patients with disc herniation. We do not have any data on PCT, or its relationship with CRP in our paper, as we did not routinely check serum PCT levels in our cohort. This work had several limitations including the retrospective study design, which may have resulted in missing key variables. Additionally, we did not collect any data on treatment and its outcomes in the patients with or without a confirmed microbiological diagnosis.

Conclusions

The likelihood of isolating a causative organism from a percutaneous CT-guided biopsy in patients with spondylodiscitis with a negative blood culture and low admission CRP is poor. Repeat percutaneous CT-guided biopsy is of limited value. Antimicrobial treatment should be started to target common causative organisms, namely *Staphylococcus spp.*, especially when presenting CRP is ≤ 50.

Conflict of interest

The authors declare no conflicts of interest

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