Infection (2019) 47:475–478
https://doi.org/10.1007/s15010-019-01294-6

BRIEF REPORT

Vertebral osteomyelitis due to *Candida* species

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Received: 3 December 2018 / Accepted: 1 March 2019 / Published online: 13 March 2019

Abstract

Objective We have noted an increased number of cases of vertebral osteomyelitis secondary to *Candida* species over the past few years at our facility. Our aim was to identify and review these cases to elucidate risk factors, treatment regimens and outcomes.

Methods We performed a retrospective chart review using our electronic medical record and microbiology laboratory database to identify cases of vertebral osteomyelitis due to *Candida* at a single teaching hospital from 2006–2018.

Results We found 15 cases of *Candida* vertebral osteomyelitis. The majority of cases were due to *Candida albicans* and affected either the lumbar or the thoracic spine. Injection drug use and previous spine surgery were the two most common risk factors identified. Treatment was largely with intravenous antifungal induction followed by prolonged therapy with oral fluconazole. There was no short-term mortality though we lacked long-term follow-up on most patients.

Conclusions The number of vertebral infections due to *Candida* may be increasing. This may be partially driven by both a rise in intravenous drug use as well as the growing rate of spine surgery. Management following currently available guidelines seems favorable, though further studies are necessary to determine the optimal treatment regimen.

Keywords *Candida* · Vertebral osteomyelitis · Diskitis · Injection drug use · *Candida* infections

Introduction

Candidal vertebral osteomyelitis and diskitis have been previously described but were once a relatively rare occurrence [1]. Overall rates of infection are difficult to determine given lack of reporting and limited case series [1, 2]. Miller and Mejicano conducted a review spanning from 1966 to 2001 finding only 59 definitive cases of vertebral osteomyelitis due to *Candida* [1]. Our institution has had a significant number of cases over the past 12 years, particularly since 2015. Risk factors for invasive *Candidal* infections include antimicrobial exposure, central catheter placement, immunocompromised status, and injection drug use. As reported from many states in the USA, we have seen an increase in injection drug use, which may be driving our relative increase in incidence of vertebral osteomyelitis due to *Candida* species [1–3]. In addition, there are scant data to guide management of these patients. We collected data on patients with culture-proven vertebral osteomyelitis due to *Candida* species over the past 12 years to determine risk factors for infection and treatment outcomes.

Methods

After approval from West Virginia University's Institutional Review Board, we utilized our electronic medical record database and microbiology lab fungal culture records to identify patients with culture-proven vertebral osteomyelitis due to *Candida* species between 2006 and 2018. Our institution is an academic medical center currently with 690 beds. We collected data on age, sex, level of vertebral involvement, comorbidities, presence of central catheter, antifungal treatment, and surgical intervention. In addition, short-term mortality and need for repeat surgery were evaluated.

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Results

In total, we identified 15 cases. Patient characteristics and species isolated are outlined in Table 1. The mean patient age was 50.8 years (range 24–76) with 8 men and 7 women. As expected, the majority of infections were due to *Candida albicans* representing 66% of isolates, followed by *C. tropicalis* (20%), *C. krusei* (6.6%), and *C. parapsilosis* (6.6%). Most infections were in the lumbar spine (eight cases) followed by thoracic (five cases), and cervical (two cases). Six patients had confirmed injection drug use and

Table 1 Patient characteristics and organism isolated

Patient	*Candida* species	Age	Sex	Antifungal	Required surgery (Y/N)	Comorbidities/risk factors	Date of recovery
1	*albicans*	51	F	Undetermined	Undetermined	Suspected IDU, smoking	2009
2	*albicans*	68	F	Fluconazole 400 mg/day × 6 weeks	Yes	Prior spine surgery, myeloma, hemolytic erythrophagocytic syndrome	09/2010
3	*albicans*	53	M	Amphotericin 3 mg/kg/day then fluconazole 400 mg/day to complete 6 weeks	Yes	Nasal drug use, Hepatitis C, DMII, prior bacterial diskitis, psoriasis, smoking, prior PICC	11/2012
4	*krusei*	76	F	Caspofungin 50 mg/day for 6 weeks	Yes	Recent paraesophageal hernia repair, abdominal wall abscess, COPD, chronic respiratory failure, CKD, hypothyroidism, afib, HTN, prior CVL	06/2015
5	*tropicalis*	40	F	Caspofungin 50 mg/day × 2 weeks, fluconazole 400 mg × 10 months	Yes	L4 fusion prior, IDU, smoking	07/2015
6	*albicans*	67	M	Fluconazole 400 mg/day indefinitely	Yes	HTN, Afib, recent lithotripsy, foot injury at work	11/2015
7	*albicans*	31	F	Caspofungin 50 mg/day for 10 days, fluconazole 400 mg daily for 12 months	Yes	IDU, recent treatment for bacterial osteomyelitis, prior PICC	05/2016
8	*albicans*	34	F	Fluconazole 400 mg/day for 12 months	Yes	C spine chordoma, hypothyroidism, erosion of hardware into pharyngeal space	10/2016
9	*tropicalis*	47	M	Caspofungin 50 mg/day × 3 days then fluconazole 400 mg/day for 6 months	No	IDU, hepatitis C, CAD, COPD	12/2016
10	*albicans*	60	M	Fluconazole 400 mg/day for 12 months	Yes	Multiple spine surgeries, HTN, prior CVL	01/2017
11	*albicans*	40	F	Caspofungin 50 mg/day for 6 weeks, fluconazole 400 mg/day indefinitely	Yes	IDU, hepatitis B & C, Factor V Leiden deficiency, bacterial endocarditis	06/2017
12	*parapsilosis*	78	M	Fluconazole 400 mg/day indefinitely	Yes	Prior spine surgery, HTN, prostate cancer, prior CVL	11/2017
13	*albicans*	45	M	Caspofungin 50 mg/day × 2 weeks, fluconazole 400 mg/day × 12 months	No	IDU, CVA, DMII, HTN	12/2017
14	*albicans*	48	M	Caspofungin 50 mg/day × 5 day, fluconazole 400 mg/day indefinitely	Yes	IDU, hepatitis C, PE, HTN, IDA, recent bacterial diskitis, CAD, prior CVL	09/2018
15	*tropicalis*	24	M	Caspofungin 50 mg/day for 2 weeks, fluconazole 400 mg/day 12 months	No	IDU, smoking, hepatitis C	09/2018

IDU injection drug use, *DMII* diabetes mellitus type 2, *HTN* hypertension, *CVA* cerebrovascular accident, *CAD* coronary artery disease, *afib* atrial fibrillation, *COPD* chronic obstructive pulmonary disease, *CKD* chronic kidney disease, *PE* pulmonary embolism, *IDA* iron deficiency anemia, *CVL* central venous line, *PICC* peripherally inserted central catheter, *LFT* liver function tests

the treating providers' notes indicated suspected use in three additional patients. Five patients had undergone prior spine surgery at some point in the past and had hardware in place, but incomplete records from other facilities prohibited from determining exact dates. All but two of the patients had been admitted to our facility with diskitis; however, many patients had been hospitalized elsewhere prior for other problems. Only two patients were diabetic and five had hepatitis C infection, but none had evidence of cirrhosis or elevation of liver enzymes on admission. No patients had a documented history of prior fungemia in our system, though we did not have records from outside facilities. Six patients had central lines placed at some point prior to discovery of diskitis; however, most were placed at other facilities. Given we lack complete blood culture data, it is unclear if this contributed to fungal diskitis. The single patient with *C. krusei* also had an abdominal wall abscess growing the same organism; however, no other patients had other sites of fungal infection. Interestingly, only one patient was definitively immunosuppressed, having been on chemotherapy for multiple myeloma. Three patients had been treated empirically for bacterial diskitis prior to isolation of yeast on biopsy culture.

Treatment regimens varied somewhat across our patient population. This could be due to differences in severity of illness, medication interactions or allergy history, or lack of infectious diseases consultation, which was absent in three patients. One patient received intravenous amphotericin followed by fluconazole. Seven patients were given caspofungin followed by fluconazole and a single patient was treated with caspofungin alone. Four patients were treated with fluconazole monotherapy. For one patient the treatment regimen is undetermined as she was treated at an outlying facility and we were unable to obtain records. Surgical intervention was required in 11 patients. All patients survived to hospital discharge. Several patients required repeat surgery, two of which were within 2 months of initial treatment. Indications for repeat intervention were wound dehiscence and need for stabilization.

Discussion

We found a relatively high number of cases of vertebral osteomyelitis and diskitis due to *Candida* species from a single, large tertiary referral hospital. Overall, our patient population varied somewhat with some patients having more than one identifiable risk factor though injection drug use and prior spinal surgery were the largest risk factors in this cohort. The prevalence of injection drug use is not surprising given its known correlation with invasive fungal disease. As well, there is an increasing incidence of IDU in West Virginia [1–4]. In fact, the rise in injection drug use in the state mirrors our increase in cases of vertebral infections due to *Candida* [4]. Given our hospital is a tertiary referral center with both neurosurgical and orthopedic spine training programs the number of patients with prior spine surgery history is not surprising either. Patients clinically improved despite the variation in treatment regimens. Current Infectious Diseases Society of America (IDSA) guidelines recommend prolonged azole therapy or either echinocandin or amphotericin for a minimum of 2 weeks followed by prolonged azole therapy for susceptible species [5, 6]. With the exception of *C.krusei*, all isolates were susceptible to fluconazole. The recommended total duration of therapy is 6–12 months [5–8]. Most of our patients were treated with prolonged therapy of 6 months minimum with some being kept on therapy indefinitely. Four patients required repeat surgical intervention. One of these was the individual who received a shorter course of therapy although it is not clear whether this was due to relapse or other indication for surgery. No patients died within 6 months of treatment; however, one patient is now deceased 12 months after initial therapy. His death was not related to spinal infection.

Our case series highlights some of the characteristics of patients diagnosed with *Candida* vertebral osteomyelitis at our facility. The mean patient age was similar to prior studies as were gender variations, which slightly favor males [2]. Previous case series have shown *Candida albicans* to be the most common infecting organism but noted increasing incidence of other *Candida* species [1–3]. *Candida albicans* represented the majority of our cases; however, we also identified several other species although unlike previous studies we found no cases of *Candida glabrata*. We estimate that nine of 15 patients (60%) had used injection drugs, which is a higher rate than we found in published literature [1, 2, 9]. The second most common risk factor in our series was prior spinal surgery; however, patients seemed to have a variety of co-morbidities that may have played a role in developing infection. Treatment was largely with intravenous antifungals initially followed by oral fluconazole in the majority of the patients, which is in line with current IDSA guidelines [5, 6]. Most of our patients required a combination of medical and surgical therapy similar to other case reports. We found no increased short-term mortality in our patients, which was our expectation based on current available studies [1–3, 10].

Conclusion

Vertebral infections due to *Candida* species were once rare but now may be increasing. Although many factors may contribute to the overall rise in cases such as increased use of central venous catheters and immunosuppression, injection drug use and spinal surgery seem to play a large role in the

increase in total cases of Candida vertebral osteomyelitis at our institution. Sadly, the United States has seen a rapid increase in substance-use disorders in recent years spurring an epidemic which has carried with it not only problems related to addiction, but also the consequences of injection drug use including severe infections. Our hospital cares for large numbers of patients who inject drugs. The increase in number of invasive *Candidal* infections at our institution mirrors that of injection drug use. In addition, there are likely more cases being treated in area hospitals not associated with the West Virginia University Health System. Spinal surgery is very common and we have a very active spine service at our institution which may account for the increase in number of osteomyelitis cases in this subgroup in our cohort. The ideal treatment for these infections is not known. The majority of our patients were treated in line with current guidelines. It is not clear if they would have had better outcomes with a different treatment regimen. In addition, given we have limited long-term follow-up data on our cohort of patients we cannot determine with certainty whether our therapy resulted in long-term, infection survival. Further research is necessary to ascertain the optimal regimen and treatment duration.

Funding None.

Compliance with ethical standards

Conflict of interest The authors have no competing interest.

Ethical approval West Virginia University Institutional Review Board approved this study.

Informed consent No informed consent was required due to the retrospective nature of this study and no patient identifying information was utilized in this publication.

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