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Microbial spectrum, patient-specific factors, and diagnostics in implant-related postoperative spondylodiscitis

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Aims

Implant-related postoperative spondylodiscitis (IPOS) is a severe complication in spine surgery and is associated with high morbidity and mortality. With growing knowledge in the field of periprosthetic joint infection (PJI), equivalent investigations towards the management of implant-related infections of the spine are indispensable. To our knowledge, this study provides the largest description of cases of IPOS to date.

Methods

Patients treated for IPOS from January 2006 to December 2020 were included. Patient demographics, parameters upon admission and discharge, radiological imaging, and microbiological results were retrieved from medical records. CT and MRI were analyzed for epidural, paravertebral, and intervertebral abscess formation, vertebral destruction, and endplate involvement. Pathogens were identified by CT-guided or intraoperative biopsy, intraoperative tissue sampling, or implant sonication.

Results

A total of 32 cases of IPOS with a mean patient age of 68.7 years (37.6 to 84.1) were included. Diabetes, age > 60 years, and history of infection were identified as risk factors. Patient presentation upon admission included a mean body temperature of 36.7°C (36.1 to 38.0), back pain at rest (mean visual analogue scale (VAS) mean 5/10) and when mobile (mean VAS 6/10), as well as elevated levels of CRP (mean 76.8 mg/l (0.4 to 202.9)) and white blood cell count (mean 9.2 units/nl (2.6 to 32.8)). Pathogens were identified by CT-guided or conventional biopsy, intraoperative tissue sampling, or sonication, and Gram-positive cocci presented as the most common among them. Antibiotic therapy was established in all cases with pathogen-specific treatment in 23 (71.9%) subjects. Overall 27 (84.4%) patients received treatment by debridement, decompression, and fusion of the affected segment.

Conclusion

Cases of IPOS are rare and share similarities with spontaneous spondylodiscitis. While procedures such as CT-guided biopsy and sonication are valuable tools in the diagnosis of IPOS, MRI and intraoperative tissue sampling remain the gold standard. Research on known principles of PJI such as implant retention versus implant exchange need to be expanded to the field of spine surgery.

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Introduction

The total number of spinal procedures being performed worldwide is continually rising and, accordingly, complications associated with the intervention including postoperative infections occur more frequently.[1–5] While spondylodiscitis is rare, making up only 3% to 5% of all osteomyelitis cases, apart from the implications for the healthcare system, scientific evidence exists for the profound impact spondylodiscitis has on patient quality of life, function, and back pain.[6] Stoop et al[7] showed that in elderly patients after haematogenous spondylodiscitis mortality

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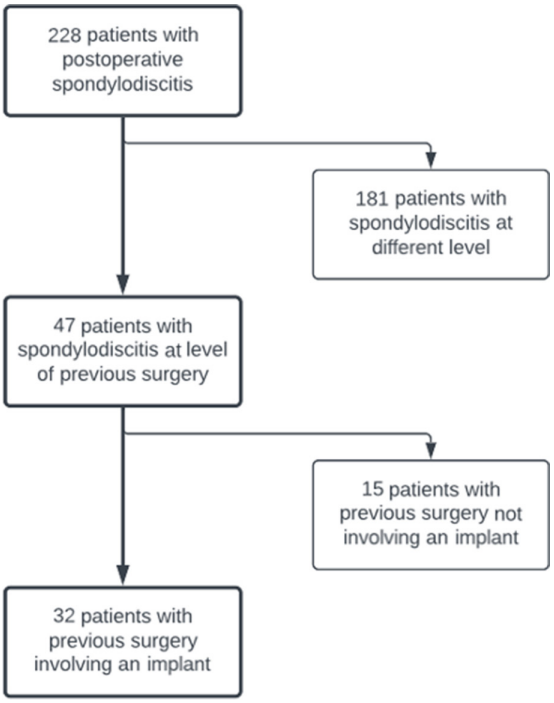

Fig. 1
Flow chart of patient inclusion.

at midterm follow-up was as high as 28% and 41% of patients reported persisting back pain of visual analogue scale (VAS) > 4.

The development of spondylodiscitis as a complication after spine surgery was investigated as early as 1998, with a statistically significant correlation between perioperative antibiotic prophylaxis and a reduced incidence postoperative spondylodiscitis (POS).[8] While some predisposing factors for the development of POS are modifiable such as obesity, smoking, or in-dwelling catheters, others such as advanced age, spinal trauma, or diabetes are not.[9,10] Apart from antibiotic therapy, measures to decrease rates of POS include the reduction of operating time and nursing staff turnover, skin cleansing baths five days prior to surgery, and the intraoperative application of antimicrobial powder.[11]

While some literature on predisposing factors exists, the overall knowledge on POS as a complication of spine surgery is still limited. Part of this may be owed to the difficulty of detecting POS in MRI early on.[12] In case of suspected infection, CT-guided biopsy proved to be a valuable tool to differentiate between neoplasia and infectious processes pre- as well as postoperatively.[13,14]

When comparing cases of postoperative with spontaneous spondylodiscitis, patients with POS tend to be younger, have a longer interval between symptom onset and diagnosis, and often require invasive diagnostic procedures.[15]

Concerning underlying pathogens, well-known agents of postoperative infections such as *Staphylococcus aureus* are found in 37% of cases with POS after lumbar discectomy.[16] Although the majority of POS cases present with bacteria typical for postoperative infections, less frequent causes such as tuberculosis or fungi infections need to be kept in mind.[17–19]

As, however, the literature on POS remains limited, our study's aim was to analyze the clinical and radiological presentation of implant-related POS (IPOS), as well as the therapeutical course and outcome.

Methods

Patients. Ethical approval was retrieved from the local ethics committee (EA1/019/21), and a retrospective analysis of patients treated for POS was carried out at a high-volume academic spine surgery centre between January 2006 and December 2020. Inclusion criteria were defined as follows: confirmed spondylodiscitis treated at our institution, history of previous spine surgery in the affected segment involving an implant, and sufficient quality of patient records. Exclusion criteria included spondylodiscitis in a segment without previous surgery, superficial and/or subcutaneous wound healing disorders, and insufficient quality of patient records.

Data retrieved included demographic data (e.g. age, sex, weight, height, risk factors), baseline data at admission (e.g. type and site of previous surgery, pain, body temperature, American Society of Anesthesiologists (ASA)[20] grade), laboratory values both at admission and discharge (e.g. CRP, haemoglobin (Hb), white blood cell count (WBC)), imaging results from MRI and/or CT scans, pathogens retrieved either from CT-guided biopsy or intraoperatively, and the performed therapeutic measures (e.g. antibiotics, revision surgery).

Spondylodiscitis was defined as typical radiological findings of the intervertebral disc both in MRI and/or CT imaging, including epidural, paravertebral, and intervertebral abscess formation, disc enhancement, vertebral destruction, and endplate involvement and correlated with clinical findings including elevated laboratory parameters for infection (CRP, WBC), reported back pain, and/or fever. The localization of the infection and previous surgery was further classified into cervical, thoracic, or lumbar. The cervicothoracic junction (C7/Th1) was defined as cervical, the thoracolumbar junction (Th12/L1) as thoracic, and the lumbosacral junction (L5/S1) as lumbar.

Radiological imaging was analyzed by an orthopaedic surgery resident (LP) trained in musculoskeletal imaging, with three years of experience in this field.

Statistical analysis. Descriptive parameters were analyzed, and means (ranges) and medians (interquartile ranges (IQRs)) were calculated where applicable. All calculations were carried out using Microsoft Excel for Mac Version 16.7 (Microsoft, USA) and IBM SPSS Statistics Version 26 (IBM, USA).

Table I. Patient demographics.

Variable	Male	Female	Overall
Mean age, yrs (range)	66.4 (37.6 to 82.7)	71.3 (58.3 to 84.1)	68.7 (37.6 to 84.1)
Mean BMI, kg/m^2 (range)	26.8 (16.4 to 41.1)	29.2 (18.7 to 47.4)	28.0 (16.4 to 47.4)
Mean length of stay, days (range)	27.5 (4 to 70)	20.6 (6 to 57)	24.3 (4 to 70)
Mean Charlson Comorbidity Index (range)	2 (0 to 10)	2 (0 to 7)	2 (0 to 10)
ASA grade	3 (1 to 3)	3 (2 to 3)	3 (1 to 3)
Risk factors, n (%)			
Smoking	4 (23.5)	1 (6.7)	5 (15.6)
Diabetes	8 (47.0)	9 (60.0)	17 (53.1)
Intravenous drug use	2 (11.8)	0	2 (6.25)
History of postoperative infection	3 (17.6)	2 (13.3)	5 (15.6)
Urinary tract infection	1 (5.9)	1 (6.7)	1 (3.1)
Cancer	2 (11.8)	2 (13.3)	4 (12.5)
Pacemaker	0	1 (6.7)	1 (3.1)
Region, n (%)			
Cervical spine	1 (5.9)	1 (6.7)	2 (6.25)
Thoracic spine	1 (5.9)	3 (20.0)	4 (12.5)
Lumbar spine	15 (88.2)	10 (66.7)	25 (78.1)
Disseminated	0	1 (6.7)	1 (3.1)
Total	17	15	32

ASA, American Society of Anesthesiologists.

Table II. Laboratory parameters.

Parameter	Admission	Discharge
CRP, mg/l	76.8 (0.4 to 202.9)	31.2 (2.6 to 123.1)
White blood cell count, units/nl	9.2 (2.6 to 32.8)	8.3 (1.9 to 36.7)
Haemoglobin, g/dl	11.1 (6.5 to 15.0)	10.5 (6.7 to 14.6)
Procalcitonin, mg/l	0.3 (0.0 to 0.9)	0.1 (0.1 to 0.3)
Albumin, g/l	33.3 (19.1 to 45.2)	31.9 (23.2 to 43.5)

All data are displayed as means and absolute ranges.

Results

Patients. We identified 228 patients presenting with spondylodiscitis. Of these, 47 had had previous surgery at the segment affected by spondylodiscitis, 32 of which involved an implant (Figure 1). In total, 17 (58.8%) patients were female and 15 (41.2%) were male. Mean age was 68.7 years (37.6 to 84.1). Two cases (6.3%) were found in the cervical spine, four (12.5%) in the thoracic spine, and 25 (78.1%) in the lumbar spine. One case (3.1%) was classified as thoracolumbar junction, while in 16 (50.0%) cases, a segment within the previous fusion was affected by the infection; in 12 (37.5%) cases, the cranial adjacent segment was affected; and in four (12.5%) cases, the caudal adjacent segment was affected. Further demographic data are presented in Table I.

Parameters at admission. Upon admission, three (9.4%) patients presented with a body temperature ≥ 37.5°C. Back pain was rated on the VAS with a mean of 5/10 at rest (0 to 10) and a mean of 6/10 during movement (0 to 10).

Neurological deficits were documented using the Frankel Scale of Spinal Cord Injury.[21] One patient (3.1%) presented with paraplegia rated as Frankel Grade A and none as Frankel Grade B. Two patients (6.3%) were rated as Grade C, showing abnormal motor function below the affected segment without practical application, and four patients (12.5%) as Grade D, with abnormal motor function but the ability to walk with or without aids. The majority of patients (78.1%) were rated as Frankel Grade E. Laboratory parameters at admission and at discharge are summarized in Table II.

Patient-specific factors. The prevalence of patient-specific factors that may contribute to infection development according to patient sex is reported in Table I. Regarding the scoring of patients in accordance to the ASA physical status classification system, one patient (3.1%) was classified as ASA grade 1 while ten patients (31.2%) scored as ASA grade 2 and the majority, 21 patients (65.6%), as ASA grade 3. The mean Charlson Comorbidity Index (CCI) among all 32 patients was two points (0 to 10).

Imaging. At least one mode of radiological imaging was performed in all patients. A total of 21 patients (65.6%) received CT and 27 (84.4%) received MRI, with 16 patients (50.0%) being subject to both. Regarding the affected segments, 21 cases (65.6%) were classified as monosegmental and 11 (34.4%) as multisegmental. L4/5 was the most commonly affected segment (nine patients, 24.3%) followed by L5/S1 (seven patients, 18.9%).

MRI revealed an epidural abscess (EA) in nine (28.1%) and a psoas abscess (PA) in ten patients (31.3%), with four patients presenting both. Five out of the nine patients with MRI-confirmed EA underwent CT scans beforehand, with no radiological findings of abscess formation.

Six out of the ten subjects with MRI-confirmed PA underwent CT scans beforehand, with two patients already presenting positive findings of PA in their CT

Table III. Radiological imaging.

Imaging finding	CT	MRI
Number of scans, n (%)	21 (65.6)	27 (84.4)
with additional MRI	16 (76.2)	N/A
with additional CT	N/A	16 (59.2)
Discal changes (enhancement), n (%)	N/A	26 (96.3)
Epidural abscess, n (%)	0	9 (33.3)
Psoas abscess, n (%)	3 (14.3)	10 (37.0)
Endplate involvement, n (%)	18 (85.7)	20 (74.1)
Vertebral destruction, n (%)	10 (47.6)	9 (33.3)

Table IV. Pathogen sampling.

Sampling method	Patients, n	Positive findings, n (%)
CT-guided biopsy	9	7 (77.8)
Open biopsy	10	6 (60.0)
Intraoperative samples	27	16 (59.3)
Sonication	5	4 (80.0)
Blood culture	11	5 (45.5)

Table V. Pathogens.

Pathogen	Cases found, n (%)
Gram-positive	
Staphylococcus epidermidis	13 (40.6)
Staphylococcus aureus	6 (18.6)
Staphylococcus lugdunensis	2 (6.3)
Corynebacterium aurimucosum	1 (3.1)
Cutibacterium acnes	1 (3.1)
Enterococcus faecalis	1 (3.1)
Enterococcus faecium	1 (3.1)
Finegoldia magna	1 (3.1)
Streptococcus agalactiae	1 (3.1)
Streptococcus sanguis	1 (3.1)
Staphylococcus warneri	1 (3.1)
Gram-negative	
Escherichia coli	1 (3.1)
Pseudomonas aeruginosa	1 (3.1)
Fungoides	
Candida albicans	1 (3.1)
Multiple pathogens	7 (21.9)

scans. Vertebral destruction was diagnosed by MRI in nine (28.1%) and by CT in ten patients (31.3%). Distribution of imaging findings between the two methods and sexes is displayed in Table III.

Pathogens, histology, and antibiotics. CT-guided biopsy was carried out in nine (28.1%) and open biopsy in ten cases (31.3%), with seven (77.8%) and six (60.0%) samples returning pathogen-positive results, respectively. Intraoperative tissue samples were taken in all 27 patients undergoing surgery, and showed positive microbiological findings in 16 cases (59.2% of patients operated on). Histological analysis was performed in 25 (78.1%) patients. Of these, 18 (72.0%) samples were positive for inflammation. In the 11 culture-negative cases, all had intraoperative histology with nine (81.8%) showing positive findings for inflammation. Of the two culture- and histology-negative cases, one had clear radiological signs of spondylodiscitis with contrast enhancement and erosive endplate changes, and the other one showed an EA in preoperative MR imaging as well as intraoperatively.

In five cases (18.5% of patients operated on) sonication of changed implant material was performed, which returned positive results in four cases (80.0%). Pathogens found and results as per mode of sampling are presented in Table IV and Table V, respectively. All patients received antibiotic therapy, 23 (71.9%) of them pathogen-specific according to sample findings and nine (28.1%) empirical.

Treatment and parameters at discharge. Five cases (15.6%) were treated conservatively and 27 (84.4%) were subject to surgical therapy. Of these 27 patients, 25 cases (92.6%) were treated by implant removal and re-fusion using a screw-rod implant of the affected segment, and two cases (7.4%) by debridement and decompression of the affected segment only. In one patient (3.1%), the affected segment had previously been fused with an interbody cage, which was then exchanged. Median time to revision surgery due to infection was 782 days (IQR 94 to 4,662).

Of the 27 patients undergoing surgery, two (6.3%) required revision within the same stay and five (15.6%) in the course of readmission after discharge (mean 199.6 days (13 to 567)). Regarding laboratory parameters at discharge, the mean CRP level was measured at 31.2 mg/l (2.6 to 123.1), mean WBC at 8.3/nl (1.9 to 36.7), and mean Hb at 10.5 g/dl (6.7 to 14.6).

Discussion

This study is one of the largest reports on patients with IPOS to date. The mean patient age of 68.7 years was older than reported by similar studies, while in accordance with the existing literature patients in our cohort had high ASA grades and comorbidities such as diabetes.[22,23]

The majority of cases (78.1%) were found in the lumbar spine, reflecting the overall distribution of spine surgeries in Germany.[24] The clinical presentation of patients on admission with only mildly elevated body temperature, back pain, and elevated CRP levels was found to be similar to reports of spondylodiscitis not related to previous spine surgery.[25,26]

Both MRI and native CT imaging proved to be valuable tools in the diagnosis of POS. The full extent of the infection, however, was missed in five out of nine CT scans of subjects with MRI-confirmed EA and in four out of six CT scans of subjects with MRI-confirmed PA, further emphasizing the importance of MRI scans in cases of suspected spondylodiscitis as showcased in Figure 2, especially in light of further improvements regarding artefact reduction in MRI.[27] Taking into account the high rate of positive findings in the patients included in our case series, it

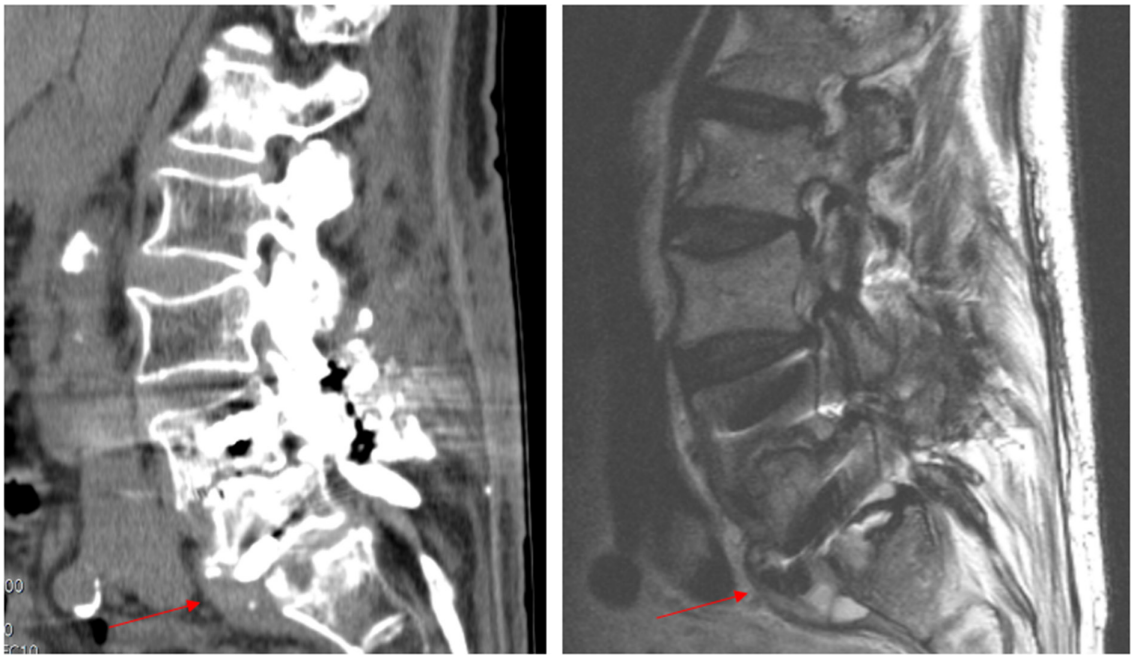

Fig. 2

Showcase of difference in visibility of paravertebral manifestations of infection in CT (left) and MRI (right). The patient was a 68-year-old female with implant-related spondylodiscitis L5/S1 and anterior abscess formation as indicated by the red arrow.

seems indispensable to perform MR imaging in patients presenting with persistent back pain after spine surgery, especially considering that most patients did not present with infection-specific clinical symptoms.

CT-guided biopsy retrieved positive samples in seven out of nine patients (77.8%), and therefore may be helpful for tailored antibiotic treatment in the majority of patients treated for POS. However, it is important to note that more than 96% of MRI-confirmed patients with spondylodiscitis would have received adequate treatment by empirical antibiotic therapy.[28] Thus, CT-guided biopsy provides additional value especially when atypical pathogens are suspected, e.g. in immunocompromised patients or potential cases of tuberculosis.[29]

The spectrum of pathogens found in this study was similar to that of periprosthetic joint infections (PJIs) of the knee and hip, with gram-positive cocci accounting for the majority of positive samples.[30–32] However, in contrast to primary spondylodiscitis, in which S. aureus has been shown to be the most common causative pathogen, in our case series *S. epidermidis* predominated which is in line with the literature on native peripheral joint infection versus PJI.[30,33–35] Furthermore, an aspect to be taken into account is recent reports on the intervertebral disc's microbiome, which may be a cause for subclinical infections as an underlying mechanism of degeneration and may predispose patients to IPOS even prior to the index surgery.[36]

Sonication delivered positive results in four out of five cases (80.0%). Analogous to CT-guided biopsy, its role in microbiological diagnosis of orthopaedic implant-related infections is disputed. The Oxford Bone Infection Unit, in one of the largest studies of its kind, found multiple tissue samplings to be more sensitive than sonication and therefore concluded that sonication should be seen as a complementary modality of diagnosis rather than an alternative to tissue sampling.[37] Furthermore, as we found histological analysis to be positive in 9 (81.8%) culture-negative patients, our results support the findings of previous studies, which indicated that histology is useful in patients with suspected spondylodiscitis.[38]

However, to date, in contrast to PJI, a clear definition and diagnostic algorithm is lacking for IPOS limiting both clinical decision-making and the comparison of treatment outcomes. As our data confirm, there does not seem to be any one diagnostic test to exclude IPOS which is why, analogous to the EBJIS criteria for the definition of PJI, a multi-step definition needs to be established.[39]

The majority of cases presented (84.4%) were treated operatively by implant removal, posterior debridement, decompression, and re-fusion using a screw-rod implant. There are currently no widely accepted guidelines on the management of IPOS. Studies on the differences in outcome of conservative versus surgical management of POS are scarce and, in most cases, based on small cohorts without control groups,[40,41] thus indicating the need for further research on this topic.

Future studies should focus on principles already evaluated and applied in the management of other PJIs

such as those of the knee and hip. With strong evidence of biofilm-active antibiotics being more effective in the treatment of implant-associated infections of the spine than non-biofilm-active,[42] the discussion of implant retention versus implant exchange needs to be brought into spine surgery too. As principles in the treatment of PJI such as two-stage revision surgeries are often not feasible due to the eminent spinal instability, the avoidance of biofilm formation is even more important. However, it is important to note that published data on IPOS are very limited and thus future studies are needed to investigate the optimal antibiotic regimen, especially in terms of duration of systemic antibiotics or antibiotic resistance, taking into account the differences in implant handling between PJI and IPOS.[43]

Following the credo 'time is implant', the management of postoperative spine implant infection (PSII) should take into account the time of infection onset, and strategies for early, delayed, and late infection need to be expanded.[44] In early infection, debridement, antibiotics and implant retention (DAIR) and biofilm-active antibiotic therapy may be viable options, which have yet to be confirmed, especially considering the conflicting data on the effect of biofilm-active antibiotics,[43,45] while in delayed and late infection implant retention may be unsuccessful and exchange needs to be considered.[46,47] As data are currently limited, it is unclear whether all implants, including intervertebral cages, or only screw-rod systems should be exchanged.[44]

This study bears the limitations that come with its descriptive and retrospective nature. There was no standardized treatment algorithm, so the choice of therapy was up to the surgeon, and the lack of a control group limits the admissible conclusions on its effectiveness. Due to the retrospective design, there is a lack of sufficient data on preoperative measures including antibiotic treatment, as well as insufficient follow-up data. Furthermore, as data were not collected prospectively, we do not have any information on the total cohort operated on during the study period, which is why a comparative analysis with a negative control group was not feasible.

In conclusion, this study represents one of the largest case series on implant-related POS available in the current literature. Although there is now a wider choice of diagnostic tools such as CT-guided biopsy and sonication, established and cost-effective methods such as MRI and intraoperative tissue sampling retain their diagnostic eminence. With growing evidence in the field of PJI, a clear diagnostic definition of IPOS is indispensable to facilitate future studies on treatment outcomes.

Take home message

- Cases of implant-related postoperative spondylodiscitis (IPOS) are rare, and share similarities with haematogenous spondylodiscitis.
- MRI and intraoperative tissue sampling should be considered the gold standard of diagnostics in IPOS.

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