BMC Infectious Diseases

CASE REPORT

Open Access

The carpal tunnel syndrome caused by *Arthrinium phaeospermum* infection: first case report and literature review

Miaozhong Li[1], Yuning Li[2] and Xueyuan Li[1*]

Abstract

Background The carpal tunnel syndrome (CTS) caused by atypical infection is a therapeutic and diagnostic challenge. Atypical clinical presentations often lead to misdiagnosis and incorrect therapy.

Case presentation This article reports a case of deep infection leading to CTS manifestations. A male patient was admitted for numbness and pain of the left hand. Left carpal tunnel release, median nerve decompression with synovial resection were performed. Inflamed synovium and effusion were submitted for bacterial culture and metagenomic next-generation sequencing (mNGS). The etiologic agent was identified as *Arthrinium phaeospermum* and the patient recovered after surgical debridement and 10 months of therapy.

Conclusions Diagnosis of mycotic infection of the hand is challenging as the presentation is similar to other conditions. mNGS is presented as a valuable diagnostic adjunct for uncovering unusual infectious agents.

Keywords *Arthrinium Phaeospermum*, Next-generation sequencing, Carpal tunnel syndrome, Infectious

Background

Carpal tunnel syndrome(CTS) is the most common peripheral nerve compression disorder, caused by idiopathic carpal transverse ligament thickening, synovial hypertrophy, etc [1]. In addition, CTS caused by secondary infection of atypical bacteria such as mycobacterium tuberculosis, non-tuberculous mycobacteria and fungi, presents a diagnostic and therapeutic dilemma. Given that the infection is rare and often fails to elicit a history of traumatic exposure [2].

Arthrinium phaeospermum is a globally distributed conditional pathogenic fungus with a wide host range, mainly in plants, and can also lead to skin lesions in humans and animals [3]. In 1990, Rai [4] reported the first case of human skin infection with this pathogen. Subsequently, four cases of human infection with *A. phaeospermum* were identified, all of them were superficial skin infections occurring in mainland China [5–8]. This article reports a case of deep infection leading to CTS manifestations, the etiologic agent was identified as *A. phaeospermum* by Metagenomic next-generation sequencing(mNGS) and culture, and the patient recovered after surgical debridement and 10 months of antimicrobial therapy. This manuscript presents a rare instance of acute CTS secondary to an infection by *A. phaeospermum*, detailing the diagnostic approach and therapeutic intervention.

*Correspondence:
Xueyuan Li
lixueyuan2000@163.com
[1]Hand Surgery Department, Ningbo No.6 Hospital, Ningbo, China
[2]Clinical Medical Laboratory Center, Ningbo No.6 Hospital, Ningbo, China

Case presentation

A 64-year-old male farmer residing in a coastal region was admitted to the hospital with a three-week history of "numbness and pain in the first through fourth fingers of his left hand." The etiology of the symptoms was not apparent, with the pain extending from the fingers to the palm and intensifying nocturnally, thereby disrupting his sleep. Despite receiving antibacterial treatment at a local hospital, there was no significant improvement observed. Medical history was unremarkable except a habit of alcohol consumption.

Physical examination showed mild swelling of the left wrist, elevated skin temperature, mild atrophy of the thenar major muscles of the left palm, tenderness over the wrist and numbness over 1–4 fingers, along with positive Tinel's sign and Phalen's test. The patient experienced limitations in finger flexion and extension movements (Figure 1). Visual analogue scale: 6 points.

Investigations

Chest, hand, and wrist X-rays revealed no specific abnormalities, as were the laboratory tests. EMG demonstrated slowed median nerve conduction velocity at the left wrist, compound muscle action potential (CMAP) amplitude of abductor pollicis brevis (APB) was reduced to 2.1 mV, compared to the normal side's amplitude of 10 mV, and the distal latency was 4.5 ms, compared to the normal side's distal latency of 4.2 ms. When stimulating the median nerve and ulnar nerve on the affected side, the difference in the latency of the sensory nerve action potentials on both sides of the 4th digit is greater than 0.4 milliseconds.

Treatment

The patient underwent surgical intervention, which included a left carpal tunnel release and a synovectomy. About 1 ml of yellow exudate was observed in the carpal tunnel. The inflamed proliferative synovium was adherent to the flexor tendons. The median nerve was compressed and flattened, with congestive changes of the epineurium. The exudate and inflammatory synovial tissue were sent for routine bacterial culture, mycobacterial culture, pathology and mNGS, respectively. Then we performed thorough debridement of the inflamed synovium. Cefoperazone Sodium and Sulbactam Sodium 1.5 g iv q12h were administered postoperatively.

Fig. 1 Before surgery, the finger flexion movement was restricted

On the second day, mNGS reported *A. phaeospermum* infection. Fungal growth was reported in the culture, consistent with the characteristics of *A. phaeospermum* later.Histopathology showed chronic synovitis with non-caseating granulomas, inflammatory cell infiltrate with proliferating capillaries (Fig. 2).but there was no fungal elements detected upon special staining.

The previous antibiotic was discontinued and Fluconazole 200 mg twice daily was initiated. At the 6-week postoperative follow-up, numbness and pain in the patient's left hand were significantly relieved. and the range of motion of fingers showed improvement compared to preoperative status. There was mild swelling of the wrist, and limited ability to make a fist (Figue 3). Two months postoperatively, the therapeutic regimen was adjusted to Terbinafine in a local hospital. There was no significant relief of wrist redness and swelling and patient complained of gastrointestinal symptoms one month later. The Terbinafine was switched back to oral Fluconazole. At the 6-month follow-up, there was only occult swelling observed in the wrist, with no evidence of disease relapse. By the 10-month follow-up, the patient had regained nearly full range of motion in the hand and was asymptomatic.(Figue 4).

Discussion and conclusions

1. Biological characteristics of *A. phaeospermum.*

A. phaeospermum belongs to the Ascomycota and can cause diseases in various plants. It is widely present in the environment. Khan et al. first confirmed it as a phytopathogenic fungus in 1980 [9]. In 2009, Zhu et al. first proved that it could lead to withering disease of hybrid bamboo [10]. It is also one of the conditional pathogenic fungi causing cutaneous fungal diseases in humans and animals. Zhao Yaoming's research confirmed that *A. phaeospermum* could infect rabbits, cavies and mice, damage hair follicles and sebaceous glands, and produce liposoluble toxins leading to skin damage [11]. In addition, Bloor [12] et al. found that *A. phaeospermum* could produce aromatic acids when infecting the human body, and Rai et al. [4] first isolated *A. phaeospermum* from the skin lesions of patients. In immunocompromised populations, fungi can occasionally cause deep hand tissue infections, which have been reported in individual cases, but *A. phaeospermum* has not been implicated. The patient had no

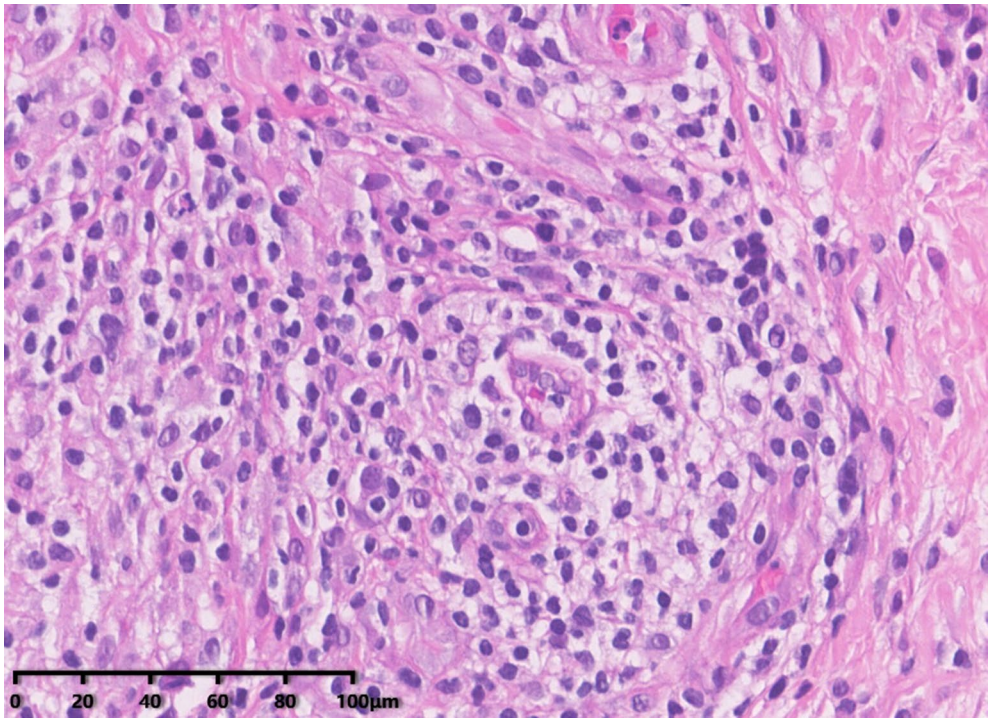

Fig. 2 There is prominent synovial hyperplasia characterized by the development of nodular structures, with a notable infiltrate comprising lymphocytes, plasma cells, and foam cells evident upon microscopic examination. The presence of these cellular constituents suggests an active inflammatory process within the synovium

Fig. 3 There was mild swelling of the wrist, and limited ability to make a fist with the fingers at the 6 weeks follow-up

Fig. 4 At the 10 month, the patient made almost full recovery of the motion rage without any symptom

other evidence of immunodeficiency except a long history of alcohol drinking.

In recent years, many studies have confirmed that it can produce various secondary metabolites and enzymatic proteins involved in pathogenesis. Li [13] et al. discovered that *A. phaeospermum* could produce a protein toxin that increases mitochondrial lipid peroxidation, inhibits respiration, and plays an important role in its pathogenicity. But the specific virulence-related genes and mechanisms of action need further in-depth study.

2. Characteristics of CTS caused by infection.

The carpal tunnel is a narrow anatomical canal. In addition to the median nerve, there are also nine flexor tendons inside the carpal tunnel cavity. Any factor that alters the structures in the carpal tunnel can compress the median nerve, leading to characteristic symptoms with pain or paresthesias in radial three and a half digits and weakness or thenar eminence muscle atrophy.

Acute or chronic local inflammation caused by infection may stimulate proliferation of the carpal tunnel

contents, compressing the nerves indirectly. Bailey [14] reported the first case of CTS due to infection. Infectious CTS is relatively rare, with most cases caused by Staphylococcus aureus, which can lead to purulent tenosynovitis and cause CTS secondarily. Mascola JR [2] reviewed, documented infectious causes of CTS, such as common bacteria, mycobacterium tuberculosis [15], atypical mycobacteria, fungi, viral and parasites. For those atypical infections(Table 1), non-specific clinical presentation may lead to misdiagnosis and delayed therapy. Most patients begin to suspect infection when they see a large amount of inflamed proliferative synovium during surgery. Moreover, special cultures take 4–6 weeks or longer, leading to a delay in treatment. After diagnosis, targeted antimicrobial treatment needs to last for months.

This patient has been taking oral fluconazole for nearly one year and eventually recovered. Currently there is no sign of recurrence. We performed mNGS of the cultured strain, and the results showed that the fungal genome contains abundant gene clusters encoding carbohydrate active enzymes, effector proteins and secondary metabolism-related genes, some of which are related to pathogenicity. It indicates that *A. phaeospermum* may have been pathogenic invasion of the tissue through its metabolic products and effector proteins.

Unlike pyogenic infections, fungal and mycobacterial infections are more likely to be overlooked in clinics. (28–29) Clinical reports of *A. phaeospermum* infection are rare. It is an opportunistic pathogen that tends to invade immunocompromised populations. This patient had nothing special but living in an area conducive to bamboo proliferation and agriculture. Given that *A. phaeospermum* can lead to withering disease of hybrid bamboo [8], it reminds us that we should increase awareness of this pathogen and strengthen fungal culture and identification of surgical samples to avoid misdiagnosis. Regarding treatment, thorough removal of inflamed synovium combined with postoperative antifungal treatment is currently the preferred therapeutic approach. When selecting antifungal drugs, hand surgeons should consult opinions from infectious disease specialists to achieve adequate therapeutic regimen [15].

3. Application of mNGS in the diagnosis of infectious diseases.

Traditional pathogen culture and morphological identification require a certain amount of time, and some pathogens are difficult to culture, causing some limitations. In recent years, the development of mNGS technology has brought new opportunities for the diagnosis of infectious diseases, and has been widely used in the detection of bacterial and viral infections [30]. Genomic sequencing can detect all pathogen information in body fluid and

Table 1 Infectious etiologies of CTS reported in literature

Year	Author	Predispoing factors	Clinical presentation	Microorganism	Treatment	Out come
2019	Jessica [16]	N/A	swelling, pain and numbness	*Mycobacterium szulgai*	Synovectomy, antibiotic therapy	well at 9 mo
2019	Li [17]	wounds, N/A	swelling, pain and numbness	Nontuberculosis mycobacteria	Synovectomy, anti-mycobacterium	6/7 well at 3 mo, 1/7 recurrence
2002	Gallagher [18]	none	swelling, pain, loss of strength	Filarial	Synovectomy	well at 2 y
2010	Sharma [19]	N/A	swelling, pain, loss of strength	Cysticercosis	Steroids, nonsteroidal anti-inflammatory drugs.	well at 2.5 mo
1981	Stratton [20]	Wood splinter trauma	Swelling, restricted motion	*Sporothrix schenckii*	Debridements, iv amphotericin B	well at 4 y
1955	Bailey [14]	trauma	Swelling, restricted motion, pain and numbnes	tuberculous infection	Synovectomy, penicillin	well at 6 mo
1991	Mascola [2]	none	swelling, pain and numbness	*Histoplasma capsulatum*	Synovectomy, ketoconazole	well at 6 mo
1963	Willians [21]	trauma	pain and numbness	Pyogenic bacteria	Debridement, penicillin and streptomycin	well at 8 mo
1988	DeHertogh [22]	N/A	pain and numbness	*Neisseria gonorrhoeae*	Amoxicillin and indomethacin	well at 3 mo
1989	Halperin [23]	N/A	numbness	*Borrelia burgdorferi*	Antibiotic treatment	well at 3 mo
1983	Sahs [24]	tampons, pilonidal sinus or N/A	swelling, pain, high fever, hypotension, vomiting, diarrhea, myalgia, headache	Toxic shock syndrome	Antibiotic therapy	well at 5 mo – 18 mo
1982	Blennow [25]	rubella virus	numbness or tingling during the night.	Rubella virus	N/A	N/A
1973	Hale [26]	rubella vaccine	numbness	Rubella vaccine	Corticosteroid	well after injection
1965	Balasubramania [27]	N/A	swelling and numbness	Guinea worm	Operation	well at 2 weeks

tissue samples by non-specific amplification and direct sequencing of all genomic DNA, enabling detection of unknown pathogens. This provides strong support for the diagnosis of infectious diseases. In this case, mNGS (Figue 5) expeditiously discovered the presence of *A. phaeospermum* in the patient's carpal tunnel synovial sample, providing crucial diagnostic data.

A. phaeospermum can cause multiple system infections in plants and animals, and its pathogenic mechanism is related to the secreted toxins and enzymes. This case suggests that *A. phaeospermum* can also stimulate synovial hyperplasia in the carpal tunnel, leading to the rare fungal CTS. Its clinical manifestations are similar to mycobacterial infections, and are very easily overlooked

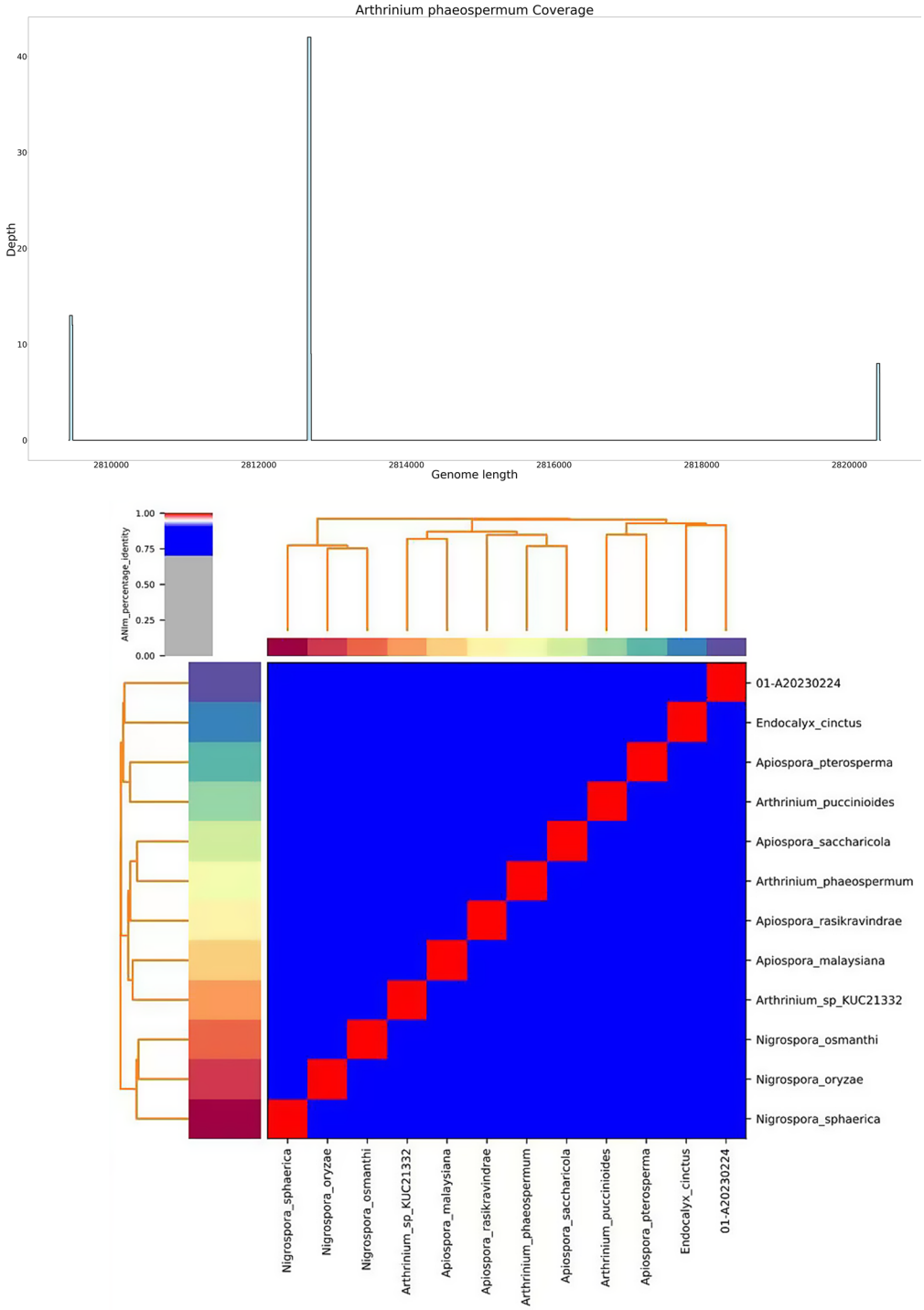

Fig. 5 mNGS result of the patient's synovium tissue. Mapping of Arthrinium phaeospermum reads to the genome community in synovium tissue sample

clinically. For abnormal inflammatory hyperplastic synovial changes found during surgery, timely bacteriological testing should be performed. The current mNGS technology technique allows rapid detection of pathogens, avoiding misdiagnosis and mistreatment.

Abbreviations

CTS Carpal tunnel syndrome
mNGS Metagenomic next-generation sequencing

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-10232-3.

Supplementary Material 1

Acknowledgements
The authors thank the workmates for their efforts in the clinical management of this patient.

Author contributions
Conception and design of the study, Operation: Xueyuan Li and Miaozhong Li. Acquisition of data: Yuning Li. Analysis and interpretation of the data: Miaozhong Li. Writing of the manuscript: Miaozhong Li. Critical revision of the manuscript for intellectual content: Xueyuan Li. All authors contributed to the article and approved the submitted version.

Funding
This study was supported by grants form the Ningbo Top Medical and Health Research Program (No.2022020506), Ningbo Key Research and Development Program (No. 2022Z146).

Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. (Data is provided within the supplementary information files).

Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the local legislation and institutional requirements which was approved by the Ethics Committee of Ningbo No. 6 Hospital. The patient provided his written informed consent to participate in this study.

Consent for publication
Written informed consent was obtained from the patient for publication of this case and any accompanying images report. A copy of the written consent is available for review by the Editor of this journal.

Competing interests
The authors declare no competing interests.

Received: 20 March 2024 / Accepted: 14 November 2024
Published online: 21 November 2024

References

1. Pai GM, Bhat AK, Acharya AM, Reddy SP, et al. Unusual presentation of carpal tunnel syndrome due to Mycobacterium marinum infection of hand. BMJ Case Rep. 2022;15(12):e251692. https://doi.org/10.1136/bcr-2022-251692.
2. Mascola JR, Rickman LS. Infectious causes of carpal tunnel syndrome: case report and review. Rev Infect Dis. 1991;13(5):911–7. https://doi.org/10.1093/clinids/13.5.911.
3. Li SJ, Tang YW, Fang XM, Qiao TM, Han S, Zhu TH. Whole-genome sequence of Arthrinium Phaeospermum, a globally distributed pathogenic fungus. Genomics. 2020;112(1):919–29. https://doi.org/10.1016/j.ygeno.2019.06.007.
4. Rai MK. Mycosis in man due to Arthrinium phaeospermum var. Indicum. First case report. Mycoses. 1989;32(9):472–5. https://doi.org/10.1111/j.1439-0507.1989.tb02285.x.
5. Zhao YM, Deng CR, Chen X, Liu ML, Chen SP, Wang Z, Sun HL. Arthrinium phaeospermum causing dermatomycosis, a new record of China. Acta Mycologica Sinica. 1990;9(3):232–5. https://doi.org/10.13346/j.mycosystema.1990.02.011.
6. Lu GX, Shen YN, Chen W, Hu SQ, Li HZ, Liu WD. Cutaneous mycosis caused by Arthrinium phaeospermum: a Case Report. Chin J Dermatol. 2005;38(4):232–4. https://doi.org/10.3760/j.issn:0412-4030.2005.04.012.
7. Hu SQ, Zhan P, Lu GX, Mei H, Zeng XS, Liu WD. A case of cutaneous arthrinium phaeospermum infection after lower limb amputation. Chin J Dermatol. 2016;49(10):726–8. https://doi.org/10.3760/cma.j.issn.0412-4030.2016.10.012.
8. Chen XW, Zhu HM, Wen H. A case of cutaneous mycosis caused by Arthrinium Phaeospermum. Chin J Mycol. 2016;11(6):357–60. ,365.
9. Khan KR, Sullia SB. Arthrinium phaeospermum var. Indicum var. nov. a new market pathogen of cowpea, garden pea and French bean. Acta Bot Ind. 1980;8:103–4. https://doi.org/10.1007/BF00121015.
10. Zhao YM, Wen ST, Liu ML, Jiang YB, Zhang SS. Mycosis caused by Arthrinium Phaeospermum, its animal toxicity and pathological analysis. Mycosystema. 1997;5:112–6. https://doi.org/10.1007/s00376-997-0061-6.
11. Bloor S. Arthrinic acid, a novel antifungal polyhydroxyacid from Arthrinium Phaeospermum. J Antibiot (Tokyo). 2008;61(8):515–7. https://doi.org/10.1038/ja.2008.69.
12. Li SJ, Liang M, Zhu TH. Selection of an antagonistic bacterium against Arthrinium phaeospermumand its antibacterial protein analysis. J Nanjing Forestry Univ. 2013;13(37):27–32. https://doi.org/10.3969/j.issn.1000-2006.2013.06.006.
13. King V, Crouser N, Speeckaert A, Bhatt R. Infection Management for the Hand Surgeon. Hand Clin. 2023;39(3):465–73. https://doi.org/10.1016/j.hcl.2023.04.003.
14. Bailey D, Carter JF. Median-nerve palsy associated with acute infections of the hand. Lancet. 1955;268(6863):530–2. https://doi.org/10.1016/s0140-6736(55)91217-4.
15. Hassanpour SE, Gousheh J. Mycobacterium tuberculosis-induced carpal tunnel syndrome: management and follow-up evaluation. J Hand Surg Am. 2006;31(4):575–9. https://doi.org/10.1016/j.jhsa.2005.01.018.
16. Jessica H, Peter R. Mycobacterium szulgai infection as a cause of carpal tunnel syndrome in a patient who kept a Mississippi mud turtle.[J]. J Hand Surg Eur Vol. 2019;44(5):543–5. https://doi.org/10.1177/1753193419829365.
17. Li XY, Jian R, Zhou XL, Li YN, Hu HL, Yu M, et al. Carpal tunnel syndrome caused by nontuberculosis mycobacteria infection. J Hand Surg Am. 2019;35(2):108–10. https://doi.org/10.3760/cma.j.issn.1005-054X.2019.02.010.
18. Gallagher B, Khalifa M, Van Heerden P, Elbardisy N. Acute carpal tunnel syndrome due to filarial infection. Pathol Res Pract. 2002;198(1):65–7. https://doi.org/10.1078/0344-0338-00187.
19. Sharma SR, Sharma N, Yeolekar ME. Carpal tunnel syndrome caused by cysticercosis. Indian J Plast Surg. 2010;43(2):210–2. https://doi.org/10.4103/0970-0358.73454.
20. Stratton CW, Lichtenstein KA, Lowenstein SR, Phelps DB, Reller LB. Granulomatous tenosynovitis and carpal tunnel syndrome caused by Sporothrix schenckii. Am J Med. 1981;71(1):161–4. https://doi.org/10.1016/0002-9343(81)90284-9.
21. Willians LF Jr, Geer T. Acute carpal tunnel syndrome secondary to pyogenic infection of the forearm. JAMA. 1963;185:409–10. https://doi.org/10.1001/jama.1963.03060050087033.
22. DeHertogh D, Ritland D, Green R. Carpal tunnel syndrome due to gonococcal tenosynovitis. Orthopedics. 1988;11(1):199–200. https://doi.org/10.3928/0147-7447-19880101-23.
23. Halperin JJ, Volkman DJ, Luft BJ, Dattwyler RJ. Carpal tunnel syndrome in Lyme borreliosis. Muscle Nerve. 1989;12(5):397–400. https://doi.org/10.1002/mus.880120510.
24. Sahs AL, Helms CM, Dubois C. Carpal tunnel syndrome: complication of toxic shock syndrome. Arch Neurol. 1983;40(7):414–5. https://doi.org/10.1001/archneur.1983.04050070044008.
25. Blennow G, Bekassy AN, Eriksson M, Rosendahl R. Transient carpal tunnel syndrome accompanying rubella infection. Acta Paediatr Scand. 1982;71(6):1025–8. https://doi.org/10.1111/j.1651-2227.1982.tb09567.x.
26. Hale MS, Ruderman JE. Carpal tunnel syndrome associated with rubella immunization. Am J Phys Med. 1973;52(4):189–94.

27. Balasubramanian V, Ramamurthi B. An unusual location of guineawonn infestation: report of a case. J Neurosurg. 1965;23(5):537–8. https://doi.org/10.3171/jns.1965.23.5.0537.
28. Fox MP, Jacoby SM. Fungal infections of the Hand. Hand Clin. 2020;36(3):355–60. https://doi.org/10.1016/j.hcl.2020.03.009.
29. Zhang KY, Yu C, Li YX, Wang Y. Next-generation sequencing technology for detecting pulmonary fungal infection in bronchoalveolar lavage fluid of a patient with dermatomyositis: a case report and literature review. BMC Infect Dis. 2020;20(1):608. https://doi.org/10.1186/s12879-020-05341-8.
30. Fang X, Yan P, Luo F, Han S, Lin T, Li S, et al. Functional identification of arthrinium phaeospermum effectors related to Bambusa pervariabilis × dendrocalamopsis grandis shoot blight. Biomolecules. 2022;12(9):1264. https://doi.org/10.3390/biom12091264.

Publisher's note