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Clinical Case of Temporal Bone Tuberculosis at Drug-Resistant Tuberculosis/HIV Co-Infection: Risk Factors, Features of Clinical Course, Treatment and Outcomes

Our own observation of a case of temporal bone tuberculosis in a patient with co-infection of drug-resistant tuberculosis/HIV infection is presented. The aim of the work was to identify risk factors, features of the clinical course, treatment and outcomes of temporal bone tuberculosis at drug-resistant tuberculosis/HIV co-infection. Analysing the clinical case, we found the following features. Injection drug addiction, self-interrupted treatment of drug-resistant tuberculosis and irregular antiretroviral therapy (ART) intake were risk factors for temporal bone tuberculosis (otitis media, mastoiditis) in the presented case. The lack of information among otolaryngologists about drug-resistant tuberculosis with bacterial excretion in the patient caused a lack of vigilance regarding the tuberculous nature of chronic epitympanic-antral purulent otitis media, which led to late diagnosis and the development of an advanced form of temporal bone tuberculosis (otitis media, mastoiditis) and Bell's palsy. The development of tuberculosis of the temporal bone (otitis media, mastoiditis) and the formation of a fibrocavernous form of a specific process in the lungs were outcomes of interrupted treatment for drug-resistant tuberculosis and irregular ART intake in case of drug-resistant tuberculosis/HIV co-infection. The features of the temporal bone tuberculosis clinical course in case of drug-resistant tuberculosis/HIV co-infection were the appointment of correct comprehensive treatment, which contributed to the cessation of bacterial excretion after 4 months, positive clinical and laboratory dynamics and healing of temporal bone tuberculosis.

Keywords

Temporal bone tuberculosis, drug-resistant tuberculosis, HIV infection.

The combined course of tuberculosis and HIV infection contributed to a change in the structure of morbidity: not only severe disseminated forms but also extrapulmonary forms of tuberculosis began to be diagnosed more often [1].

Tuberculous mastoiditis is one of the rare forms of extrapulmonary tuberculosis (EPTB), and destruction of the mastoid process of the temporal bone and auditory ossicles may develop when it is left untreated, leading to intracranial spread of the infection [2, 10]. Mastoiditis is often a complication of otitis media [3, 4, 8], and timely antimycobacterial therapy (AMBT) contributes to the resorption of abscesses and the healing of tuberculous mastoiditis [9]. There is a recommendation that for prolonged otitis media, the possibility of a tuberculous aetiology of the disease should be considered if there is a poor or absent response to nonspecific antibiotic therapy [3, 5, 6].

Diagnosis of temporal bone tuberculosis is difficult, especially if it is a primary process, and the diagnosis is mainly confirmed by the presence of *Mycobacterium tuberculosis* (MTB) in abscess secretions and histological examination of postoperative material [2, 4, 5, 7].

M. Guan et al. noted the difficulty of diagnosing tuberculous otitis media [6], describing a clinical case in which a 49-year-old woman was underwent

four operations with a diagnosis of «chronic purulent otitis media», after which left-sided Bell's palsy developed. Only after a long time were secretions from the ear analysed for MTB, which allowed the diagnosis of the tuberculous nature of the inflammatory process to be made.

As you can see, tuberculosis of the temporal bone is a pathology that is very difficult to diagnose, especially given the of lack of vigilance among physicians regarding this disease. At the same time, we did not find data on the course of temporal bone tuberculosis in cases of drug-resistant tuberculosis/HIV co-infection in the literature, which makes this work relevant.

Objective — to identify risk factors, features of the clinical course, treatment and outcomes of temporal bone tuberculosis at drug-resistant tuberculosis/HIV co-infection using our own case as an example.

Clinical Case

Patient *Serhii M.,* 48 years old.

Disease history: The diagnosis of HIV infection was made in January 1998, antiretroviral therapy (ART) was prescribed since April 2013, the latest ART regimen: TDF/3TC/DTG. The patient suffers from injection drug addiction. Dynamics of the number of CD4 lymphocytes (LF) and viral load (VL): 2013 year — CD4-LF 42 cells (10.6 %) and VL — 664 058 RNA copies/mL, 2014 year — CD4-LF 106 cells (12.0 %) and VL < 40 RNA copies/mL, 2015 year — CD4-LF 226 cells (19.9 %) and VL < 40 RNA copies/mL, 2016 year — VL < 40 RNA copies/mL, 2017 year — CD4-LF 596 cells (36.1 %), 2023 year — CD4-LF 345 cells (32.5 %) and VL < 40 RNA copies/mL.

In 2020, he underwent a course of treatment for chronic viral hepatitis C according to the SOF/VEL regimen. Pulmonary tuberculosis was first detected in March 2017: during treatment phenotypic drug susceptibility testing (phDST) revealed MTB that were resistant to the following antimycobacterial drugs: isoniazid (H), rifampicin (R), ethambutol (E), streptomycin (S), kanamycin (Km), capreomycin (Cm), amikacin (Am), ofloxacin (Ofx), levofloxacin (Lfx), moxifloxacin (Mfx). Therefore, the case was re-registered in Pre-XDR-TB in May 2017. Based on this, treatment according to the DST data was prescribed, but patient interrupted the treatment himself in October 2017. Therefore, the patient was transferred to palliative treatment with the following diagnosis: Pre-XDR-TB (05.2017) infiltrative form of the right lung with contamination. Destruction+. MBT+, molecular genetic test (MG)+, rifampicin-resistant (Rif)+, sputum microscopy (M)+, culture (C)+, phDST (HRESKmCmAmOfxLfxMfx). Resistance—(cycloserine (Cs), para-aminosalicylic acid (Pas)). Histology 0 (Palliative treatment). HIV infection, IV clinical stage.

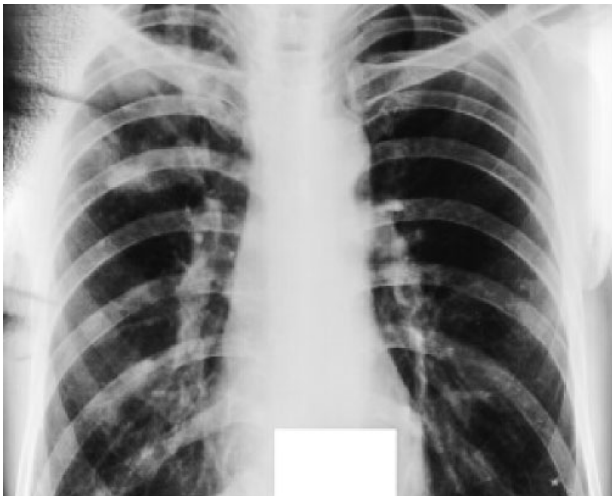

Fig. 1. **Chest X-ray from November 2023**

Since July 2023, the patient has suffered from chronic epitympanic-antral bilateral purulent otitis media. He repeatedly received conservative treatment from an otolaryngologist, but bilateral mixed conductive and sensorineural hearing loss developed.

In November 2023, a chest X-ray (X-ray) showed focal infiltration with destruction up to 2 cm in diameter in the upper lobe of the right lung (Fig. 1).

In March 2024, right-sided Bell's palsy developed during an exacerbation of chronic otitis media. A CT scan of the brain without contrast revealed signs of cerebral atrophy with vicarious expansion of cerebrospinal fluid spaces, bilateral otitis media and mastoiditis.

On 12 March 2024, a surgical intervention was performed — a separate attico-antrotomy on the right side. It should be noted that during hospitalisation in the otorhinolaryngology department, the patient denied tuberculosis and only admitted that he was suffering from HIV infection and drug addiction. In April 2024 the patient underwent secondary suturing on the incision behind the ear.

In June 2024, the patient's general condition sharply worsened and became more severe, which was manifested by severe intoxication, facial asymmetry, significant hearing loss in both ears and dryness of the right eye. The number of CD4-LF cells was 226 cells (26.4 %) and the VL was 76 RNA copies/ml. Negative dynamics on the X-ray were determined (Fig. 2): there were focal infiltrations, connected in some areas with decay cavities from 1 to 7 cm in diameter throughout the right lung; there were few foci of contamination in the upper lobe of the left lung; the roots of the lungs were infiltrated with little structure.

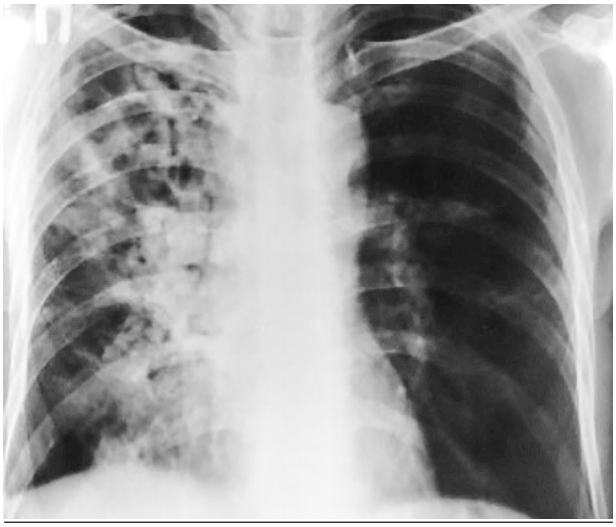

Fig. 2. **Chest X-ray from 18 June 2024**

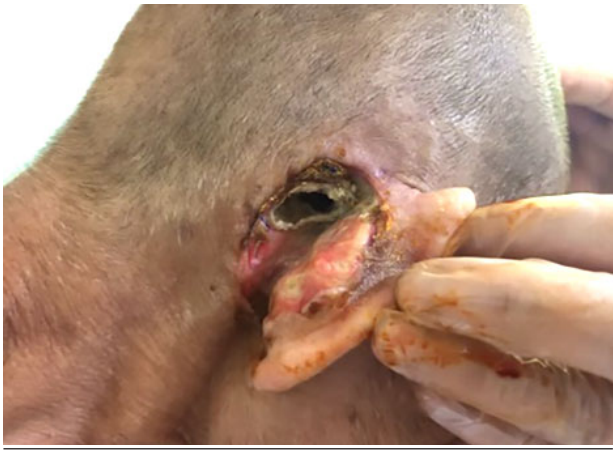

Fig. 3. **Postoperative cavity with signs of purulent-necrotic inflammation in the right postauricular area**

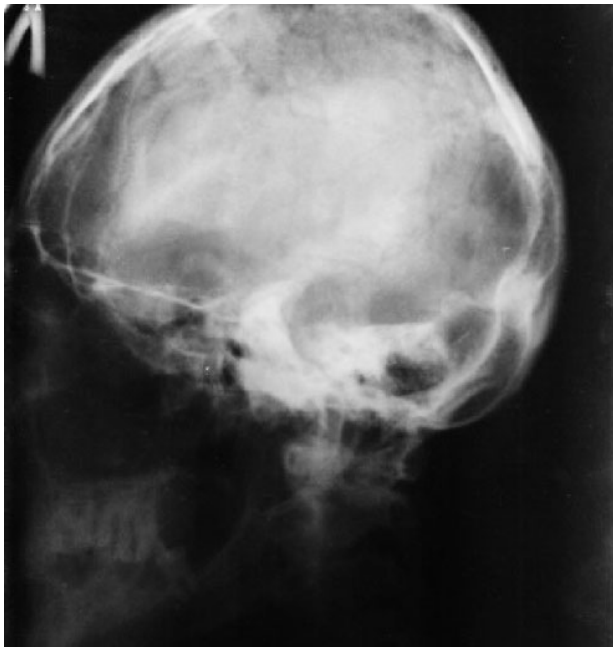

Fig. 4. **Lateral cranial X-ray from 21 June 2024**

On 20 June 2024, the patient was hospitalised in the pulmonary tuberculosis department in serious condition, where he was thoroughly examined.

First of all, the patient was examined by an otorhinolaryngologist. On examination, a postoperative cavity with signs of purulent-necrotic inflammation was identified in the right postauricular area, the sutures had failed (Fig. 3). There was a central perforation of the right tympanic membrane, paresis of the right side of the face. The next diagnosis was made: chronic right-sided otitis media complicated by facial paresis; condition after antrotomy.

Ophthalmologist's conclusion: Lagophthalmos (Bell's palsy) on the right side.

The lateral cranial X-ray dated 21 June 2024 (Fig. 4) revealed oedema and a low horizontal fluid level in the petrous part of the temporal bone.

Rapid tests for VG-C and HBsAg were negative.

During hospitalisation, the patient's biochemical blood tests, including liver function tests, glucose, potassium, sodium and chlorine, were within normal limits. However, creatinine levels were elevated, while blood urea nitrogen levels were markedly reduced.

A complete blood count revealed an response, with an elevated erythrocyte sedimentation rate (65 mm/h) and, leukocytosis (25.8×10^9/l), along with a left shift of neutrophils towards band forms.

Infectious disease specialist's conclusion: HIV infection, clinical stage IV, HIV-associated nephropathy. ART regimen: TDF/3TC/DTG was prescribed.

In the general sputum analysis, leukocytes were present in all visual field (v/f), bronchial epithelium cells numbered 10—15 per v/f, alveolar cells accounted for 1/2 of v/f, no atypical cells were detected, no pneumocysts were observed.

During the bacteriological examination of secretions from the area skin, soft tissues and temporal bone defect on the right, dated 24 June 2024, MTB was detected: M(3+) MG+ Rif+, genotypic drug susceptibility test (gDST) (HAmKmCm), C (+), phDST (HRLfxMfx0.25). Resistance— (Mfx1.0, bedaquiline (Bdq), linezolid (Lzd), clofazimine (Cfz), delamanid (Dlm)).

On 26 June 2024, a lumbar puncture was performed with cerebrospinal fluid examination: MTB– (MG–, M–), protein — 0.264 g/L, Nonne—Appelt reaction (+), Pandy's reaction (2+), cytosis — 8 cells/μL, glucose — 2.58 mmol/L, chlorides — 98.9 mmol/L, lymphocytes — 2 cells, neutrophils — 6 cells, cryptococci — not detected.

Consultant neuropathologist's conclusion: Toxic encephalopathy, right-sided facial nerve neuropathy.

Considering the additional examination data, the clinical diagnosis was made: Pre-XDR-TB infiltrative form of the right lung with contamination.

Destruction+. MTB+ MG+ Rif+ M– phDST (HRESKmCmAm OfxLfxMfx). Resistance– (CsPas). Extrapulmonary TB of the right temporal bone (otitis media, mastoiditis). Destruction+. MTB+ MG+ Rif+, gTMCH (HAmKmCm), C+, phDST (HRLfxMfx0.25). Resistance– (Mfx1.0BdqLzdCfzDlm). Histology 0 (Repeated course of treatment). Condition after surgery — separate attico-antrotomy on the right side. HIV infection, IV clinical stage. HIV-associated nephropathy. Encephalopathy of mixed genesis. Anaemia of a chronic patient. Lagophthalmos (Bell's palsy) on the right.

Complex treatment was prescribed:

- AMBT according to the individual treatment regimen (ITR) scheme, considering DST data: BdqLzdCfzCsDlmMpnAmx/Clv-//-BdqLzdCfz CsDlm;
- ART: TDF/3TC/DTG; prevention of opportunistic infections with *Biseptol* (Sulfamethoxazole and trimethoprim) and fluconazole;
- wound dressings and sanitation with 3 % hydrogen peroxide solution and betadine;
- nonspecific antibiotic therapy (ceftriaxone, ciprofloxacin, meropenem, amoxiclav).

In the sputum analysis cultured on Sabouraud Dextrose Agar dated 26 June 2024, growth of *Candida albicans* at 10^5 CFU/mL was detected. It was resistant to nystatin, fluconazole, itraconazole and clotrimazole, but sensitive to ketoconazole. No growth of non-specific bacterial microflora was observed.

After one month of inpatient treatment, the patient's bacterial excretion from secretions in the area of the defect of the skin, soft tissues and temporal bone on the right decreased from M (3+) to M (2+), the intensity of intoxication syndrome diminished and creatinine level decreased. X-rays revealed the formation of fibro-cavernous tuberculosis of the right lung (Fig. 5). The right lung was reduced in volume due to gross pneumofibrosis, there was a cavity up to 10 cm in diameter; pericavitary decay cavities ranged from 1.5 to 2.5 cm in diameter; there are polymorphic foci, sometimes of a connected nature in S6 and the lower lobe; the sinus was small, with pleural adhesions; the right hilum was fibrotically altered and pulled up; the foci had partially resolved in the upper lobe on the left; the heart was pulmonary.

Thanks to AMBT, after 3 months of inpatient treatment, the bacterial excretion both in sputum and from secretions in the area of the skin defect, soft tissues and temporal bone on the right was reduced to M (1+). Objectively, positive dynamics were observed in the form of healing of the postoperative cavity and disappearance of purulent-necrotic inflammation in the right postauricular area (Fig. 6).

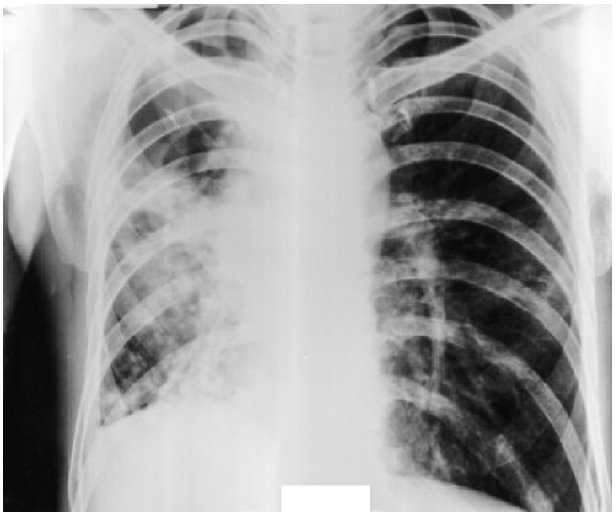

Fig. 5. **Chest X-ray after one month of inpatient treatment**

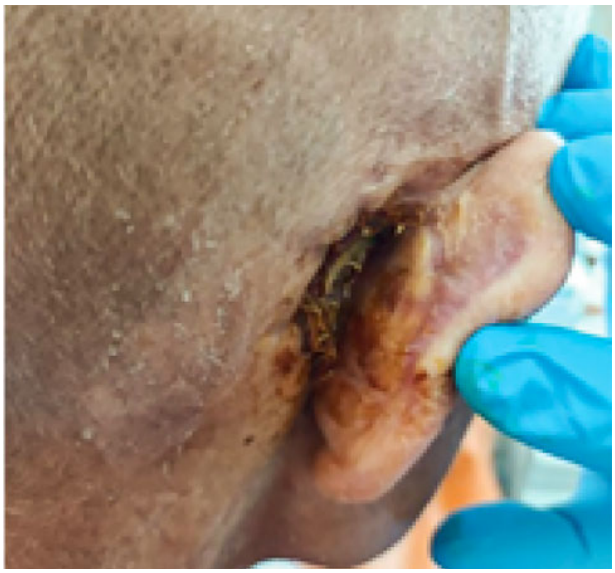

Fig. 6. **Healing of the postoperative cavity in the right postauricular area**

A negative sputum culture and positive clinical and laboratory dynamics were observed (disappearance of intoxication symptoms, normalisation of biochemical blood parameters and clinical blood analysis indicators after 4 months of treatment. Radiologically, further formation of fibro-cavernous tuberculosis of the right lung was noted (Fig. 7). The right lung was significantly reduced in volume; the upper lobe was almost completely destroyed, containing a cavity measuring 11 × 6 cm in diameter; focal dissemination was present in all lung fields; the hila were deformed, poorly structured; the right sinus was obliterated; the mediastinal organs were shifted to the right.

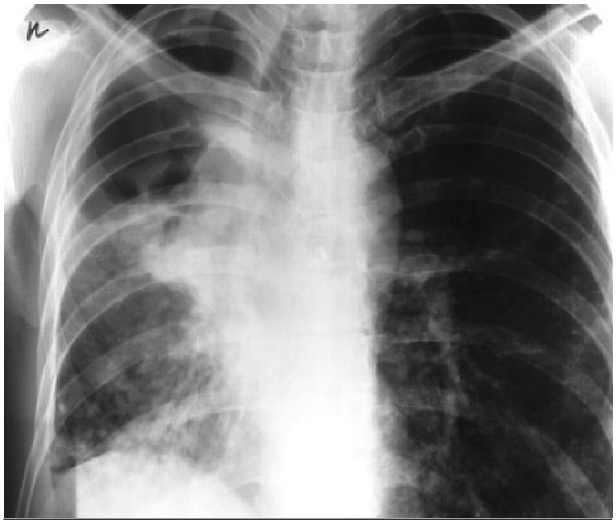

Fig. 7. **Chest X-ray after 4 month**

After obtaining a negative sputum culture, the patient was discharged for outpatient treatment.

Conclusions

1. Injection drug addiction, self-interrupted treatment of drug-resistant tuberculosis and irregular ART intake were risk factors for temporal bone tuberculosis (otitis media, mastoiditis) in the presented case.
2. The lack of awareness among otolaryngologists regarding drug-resistant tuberculosis with bacterial excretion in the patient caused a lack of vigilance regarding the tuberculous nature of chronic epitympanic-antral purulent otitis media, leading to late diagnosis and the development of an advanced form of temporal bone tuberculosis (otitis media, mastoiditis) and Bell's palsy.
3. The development of tuberculosis of the temporal bone (otitis media, mastoiditis) and the formation of a fibro-cavernous form of the specific process in the lungs were outcomes of interrupted treatment for drug-resistant tuberculosis and irregular ART intake in the case of drug-resistant tuberculosis/HIV co-infection.
4. The features of the clinical course of temporal bone tuberculosis in the case of drug-resistant tuberculosis/HIV co-infection included the prescription of appropriate comprehensive treatment, which contributed to the cessation of bacterial excretion after 4 months, positive clinical and laboratory dynamics and healing of temporal bone tuberculosis.

There is no conflict of interest.
Participation of authors: research concept and design — O.M. Raznatovska, V.I. Petrenko, O.S. Shalmin; collection of material — A.V. Fedorets, A.O. Svitlitsky, A.O. Mykhailova, O.A. Svitlytska; data analysis — O.M. Raznatovska, V.I. Petrenko, O.S. Shalmin; writing the text and statistical data processing — O.M. Raznatovska, R.M. Yasinskyi; editing of the text — O.M. Raznatovska, V.I. Petrenko.

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Клінічний випадок туберкульозу скроневої кістки при ко-інфекції лікарсько-стійкий туберкульоз/ВІЛ-інфекція: чинники ризику, особливості клінічного перебігу та лікування, наслідки

Представлено власне спостереження випадку туберкульозу скроневої кістки в пацієнта при ко-інфекції лікарсько-стійкий туберкульоз/ВІЛ-інфекція. Метою роботи стало встановити чинники ризику, особливості клінічного перебігу та лікування, наслідки туберкульозу скроневої кістки при ко-інфекції лікарсько-стійкий туберкульоз/ВІЛ-інфекція. Установлено, що чинниками ризику розвитку туберкульозу скроневої кістки (середній отит, мастоїдит) у представленому випадку були ін'єкційна наркоманія, самовільно перерване лікування лікарсько-стійкого туберкульозу, нерегулярний прийом антиретровірусної терапії (АРТ). Відсутність інформації в оториноларингологів про наявність туберкульозу з бактеріовиділенням у пацієнта спричинило відсутність настороженості щодо туберкульозної природи хронічного епітимпано-антрального гнійного середнього отиту, що призвело до пізньої діагностики та розвитку запущеної форми туберкульозу скроневої кістки (середній отит, мастоїдит) і паралічу Белла. Наслідками перерваного лікування лікарсько-стійкого туберкульозу та нерегулярного прийому АРТ при ко-інфекції лікарсько-стійкий туберкульоз/ВІЛ-інфекція були розвиток туберкульозу скроневої кістки (середній отит, мастоїдит) і формування фіброзно-кавернозної форми специфічного процесу в легенях. Особливостями клінічного перебігу туберкульозу скроневої кістки при ко-інфекції лікарсько-стійкий туберкульоз/ВІЛ-інфекція було призначення правильного комплексного лікування, що сприяло припиненню бактеріовиділення через 4 міс, позитивній клінічно-лабораторній динаміці, загоєнню туберкульозу скроневої кістки.

Ключові слова: туберкульоз скроневої кістки, лікарсько-стійкий туберкульоз, ВІЛ-інфекція.

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