Katarzyna Guziejko, Piotr Czupryna, Anna Moniuszko, Sambor Grygorczuk, Maciej Kondrusik, Joanna Zajkowska, Sławomir Pancewicz

TUBERCULOUS MENINGITIS – A CASE REPORT

Department of Infectious Diseases and Neuroinfections
Medical University in Białymstok

ABSTRACT

In this paper we present a case of a 58 years old male with a rare form of extrapulmonary tuberculosis – tuberculous meningitis (TBM). Tuberculous meningitis is usually caused by hematogenous spread of *Mycobacterium* from lungs. The TBM is a severe disease with high mortality. The symptoms usually increase gradually and in the course of the disease 3 clinical stages (prodromal phase, phase of neurological symptoms and phase of paresis) may be differentiated. Cerebrospinal fluid examination, chest x-ray and sputum culture are crucial for diagnosis of TBM. The proper diagnosis and early causative treatment significantly improve the outcome of the disease.

Key words*: extrapulmonary tuberculosis, tuberculous meningitis*

In Poland for many years there has been a steady decline in tuberculosis incidence, this is among many reasons mainly due to improved life conditions of Polish population such as better nutrition, higher standards of sanitation, as well as effective chemotherapy and tuberculosis eradication programs (1). In 2009 the incidence rate of all forms of TB amounted to 21.6 per 100,000 inhabitants, which rates Poland in a group of European countries with average TB incidence rate (2).In 2008 TB mortality rate in Poland amounted to 2.1/100,000 population (3). Although the extrapulmonary type of TB is rare (in 2009 incidence rate amounted to 1.5/100,000 population) it must be taken into consideration during differential diagnosis of disorders of other organs and systems (2). One type of extrapulmonary tuberculosis characterised by severe course of the disease and high mortality is tuberculous meningitis (TBM). The disease develops as a consequence of mycobacterium blood borne dissemination from TB primary focus most often localised in lungs. In approximately 40-50% of patients with identified TBM chest x-ray shows miliary changes, or old tuberculosis lesions (4,5).

The development of the disease is insidious, following phases can be differentiated (6.7).

I. Prodromal symptoms such as malaise, mild fever, loss of appetite, headache, which are not typical, and their duration may extend to several weeks.
II. Neurological symptoms which include lethargy, progressive cognitive disorders, cranial nerve palsy (usually oculomotor) and meningeal signs.
III. Paralysis with concomitant coma, increase in intracranial pressure, and subsequent increase in intracranial fluid space.

Not typical clinical course with slowly increasing symptoms and often mildly expressed meningeal signs, contributes to late diagnosis, and delayed implementation of a specific treatment, which significantly worsens the prognosis. TBM, if left untreated usually leads to death. Despite the availability of effective and specific treatment, the outcome of the disese may be fatal, which is the consequence of late or unrecognised tuberculous process.

We present a case study of a patient with miliary tuberculosis, as well as TBM, who was hospitalised in Department of Infectious Diseases and Neuroinfections of Medical University in Bialystok, and in whom the diagnosis of TB was given at a time of symptoms appearance suggesting central nervous system involvement.

DESCRIPTION OF THE CASE

A 58 year old patient (farmer) who for 6 months was under care of Pulmonary clinic, because of persistent productive cough, loss of body weight (25kg) and weakness, was admitted to the Department of Infectious Diseases and Neuroinfections on the 1/09/11 with suspected encephalitis. On an x-ray performed a month prior, there

Table I. Results of cerebrospinal fluid examination

Doba leczenia	**Ocena makroskowpowa**	**Cytoza (**kom/ul)	**Białko** (mg/dl)	**Albumina** (mg/dl)	**Odczyn Nonne Appelta**	**Odczyn Pandyego**	**Glukoza** (mg/dl)
2	Wodojasny, klarowny	45 (Neutrofile-81; Limfocyty-9%)	79,9	47	+	++	23
20	Wodo jasny, klarowny	14 (Neutrofile-7%; Limfocyty-66%)	40	24,7	-	+	53
60	Wodo jasny, klarowny	11	31,2	18,3	-	-/+	46

was visible presence of a shadow in left lung -apical upper lobe (suspected TB). Between 31/08/- 1/09/11 the patient was hospitalised in an Internal Disease Unit at a District Hospital due to worsening headaches, especially in the parietal area, motor aphasia, and difficulty with movement. Because of increasing cognitive decline, and the appearance of meningitis symptoms, on the second day of hospitalisation the patient was referred to the Neurological admission room with suspected hemorrhagic stroke. CT examination scan revealed only widening of the ventricles. The patient was referred to our Department with a suspicion of encephalitis.

On admission the patient was conscious, with psychomotor agitation, without logical contact and with body temperature of 38.8˚C. On GCS he scored 10 points. Physical examination revealed : neck stiffness 4cm, positive bilateral Kerning's sign, positive right side Oppenheim's sign, dehydration, quiet vesicular sound, palpable left supraclavicular node, as well as inguinal nodes and dental decay. Laboratory tests revealed elevated inflammatory parameters (CRP- 35.9mg/l, ESR-58/70, WBC- 10k), mild hyponatraemia (131mmol/l). In the next 24 hours lumbar puncture was performed. Cerebrospinal fluid (CSF) examination revealed polinuclear pleocytosis, elevated protein concentration and low glucose level (Tab.1.). Due to abnormalities observed on the chest x-ray indicating miliary tuberculosis (Fig.1.) antituberculotic treatment was commenced (Rifampicin 600mg/d, Pyrazinamid 1500/d, Nidrazid 300mg/d, Streptomicin 1.0/d). In addition antioedematous drugs were used (Mannitol 20%) and glucocorticosteroids (Dextamethasone 16mg/daily in decreasing doses for the entire duration of hospitalisation). In 3 consecutive induced sputum examinations, acid resistant bacilli was present, additionally in culture system BacT/ALERT as well as in LJ medium elevated level of mycobacteria was found. Furthermore csf (sample taken within the first 48 hours) of hospitalisation, bacteria culture after 38 days acid resistant mycobacteria grew. During the hospitalisation the patients' neurological symptoms improved. After 19 days of antituberculotic treatment control csf examination indicated normalisation of CSF parameters (Tab.1.). Patient was discharged home after 23 days of hospitalisation in general good health with recommendation to continue treatment in a Lung Diseases and Tuberculosis Unit in the District Hospital.

After 7 weeks and modification of treatment with two drugs (Rifampicin with Isoniazid) the patient was admitted to our Department for a check-up. During the admission the patient presented in general good health, without any abnormalities in physical examination. Chest x-ray revealed gradual remission of miliary changes (Fig. 1). Patient was discharged home in general good condition with recommendation to continue antituberculotic treatment (Rifamazid 300+150) in outpatient clinic and a follow up check-up in Lung Diseases and Tuberculosis Clinic in his place of residence.

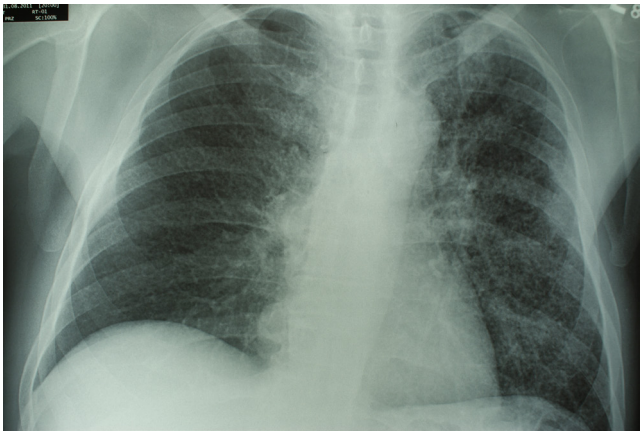

Fig. 1. Miliary tuberculosis

DISCUSSION

TBM is a rare form of extrapulmonary tuberculosis (2). The disease develops slowly, and is difficult to diagnose, because it does not manifest itself initially with characteristic symptoms. In the discussed study the disease progressed in 3 typical for TBM phases (6, 7). The condition of the patient deteriorated significantly with the emergence of subsequent symptoms proving the progression of the disease, and the prognosis for total recovery, without significant neurological deficits depended on the time of antituberculotic treatment implementation.

In differential diagnosis different etiological factors were taken into consideration, which could have caused tuberculous meningitis and encephalitis (viruses, bacte-

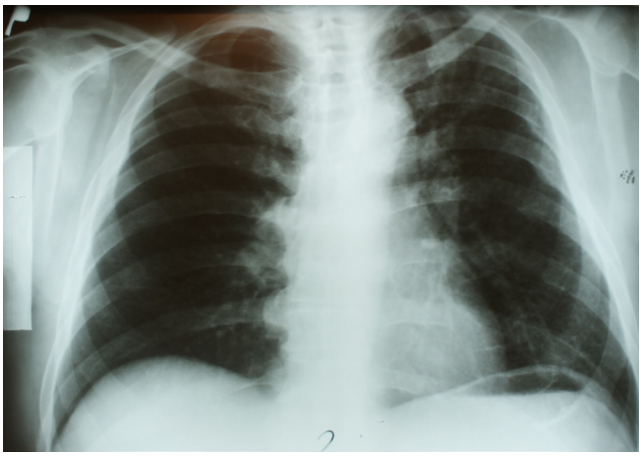

Fig. 2. Miliary tuberculosis – partial regression of changes

ria). CSF test plays a vital role in suspected tuberculosis etiology. CSF lymphocytosis, elevated concentration of proteins, and reduced concentration of CSF glucose suggest diagnosis. In CSF examination at the beginning of the patients hospitalisation, in addition to typical deviations in protein and glucose levels, polinuclear pleocytosis was found, which can occur in the initial phase of the disease (10). Glucose concentration in CSF (23mg/dl) fully met the criterion level of less than 60% of the concentration in the blood serum (94mg/dl). The growth of *Mycobacterium tuberculosis* in culture of the CSF sample is still the best standard in diagnosis of tuberculosis. Unfortunately, traditional microbiological tests have low sensitivity and long waiting period for positive results, while new and faster molecular tests (bacterial DNA amplification by PCR) remain expensive and inaccessible in routine hospital diagnosis. Although these tests have positive predictive value and high specificity, their sensitivity in diagnosis of extrapulmonary tuberculosis is hardly satisfactory. This is most likely due to low concentration of mycobacteria in CSF, insufficient volume of test material (CSF), and the presence of inhibitory substances in the process of bacterial DNA amplification. Due to this, negative test results do not exclude TBM. Taking into account the above mentioned factors, molecular tests should be performed along with the traditional microbiological studies (12, 13). Bacteriological infection confirmation and thus defined time necessary to obtain tubercular mycobacteria growth, (depending on medium, sometimes up to 2 months) should not delay appropriate therapy if there is a clear clinical rationale suggestive of TBM. Imagining tests (CT, MR) of CNS are helpful in assessing the severity of the disease, and qualification of the patients for life saving medical procedures (severe hydrocephalus). In the course of TBM CT scan of the head usually reveals in at least half of the patients widening of ventricles, abnormalities on the base of the brain and cerebral infarctions. Less frequently tuberculoma, or oedema of the brain are observed . MR of the head is more sensitive in imaging of CNS inflammation lesions (meningeal enhancement) in the TBM compared to CT scan (4, 14). In approximately 50% of patients with TB there are also tuberculous lesions in the lungs, so x-ray of the chest as well as microbiological sputum test, remain an essential part in diagnostic process.

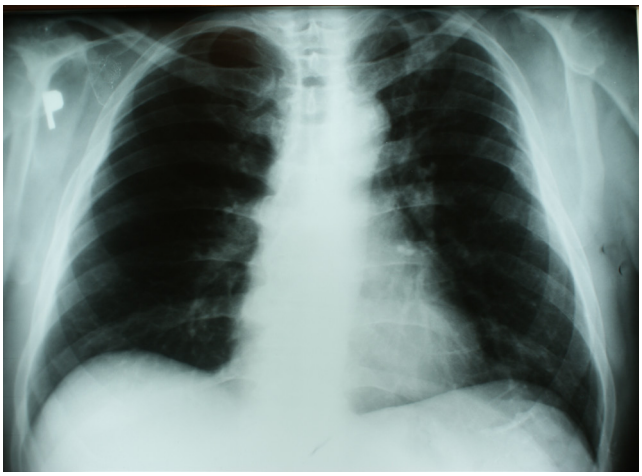

Fig. 3. Miliary tuberculosis – after 2 months of treatment

On a basic of the chest x-ray and patients history, it was decided to commence specific therapy. The choice of right combination of antituberculotic drugs as well time of TBM treatment, should cover intensive 4x drug treatment (Isoniazid INH, Rifampicin RMP, Pyrzinamid PZA, and Streptomycin SM), which continuation will be two drug maintenance therapy (INH+RMP) for 12 months. Administration of glucocorticoids (Dexamethasone) favourably influences revisable changes in CSF as well as greatly increases survival of patients. They should be administered sequentially over a period of 6-8 weeks in decreasing doses. Glucocorticoid therapy has no effect on the incidence rate of late consequences of neurological disorders (6, 15, 16, 17). On the third day of the specific therapy one could observe overall improvement in a patient's well being, as well as regression of neurological symptoms. Check-up examination on the 19th day of therapy showed tendency towards normalisation of parameters csf. After 2 months of treatment with 4 drugs (INH+RMP+PZA+SM), two drug therapy was maintained (INH+RMP). Check-up chest x-rays showed gradual remission of lung changes.

As previously mentioned, tuberculous meningitis and encephalitis occur rarely, but it should be taken into consideration in differential diagnosis of neuroinfection. Early diagnosis and commencement of specific therapy determines survival of the patient.

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Address for correspondence:
Lek. Katarzyna Guziejko
Department of Infectious Diseases and Neuroinfections
Medical University in Białystok
14 Żurawia Str.15-540 Białystok
Tel. 85 74 -09- 514, fax 85 74-09-515
e-mail: kguziejko@wp.pl