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RESEARCH ARTICLE

CLINICAL FEATURES, SEROLOGICALPATTERNS AND LONG-TERM COMPLICATIONS OF 22PATIENTS WITH NEUROBRUCELLOSIS.

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Abstract

Background:- Neurobrucellosis is an endemic zoonotic infection in Saudi Arabia and many parts of the Middle East. The diagnosis of neurobrucellosis poses a challenge to the treating physicians due to the significant variability of its presentation. Different laboratory investigations and treatment regimens have been implemented to diagnose and manage the disease. Since neurobrucellosis is both curable and potentially preventable, the degree of suspicion for neurobrucellosis should be high especially in endemic areas. The aim of our study is to show the different clinical presentations, laboratory findings,complications and different outcomes of neurobrucellosis in our society.

Method:-A retrospective analysis of the medical charts of 22 neurobrucellosis patients at King Abdulaziz Medical City (KAMC) in Riyadh during the period between 1995-2010 was carried out.

Results:- Fever was the dominant symptom seen in sixteen (73%) patients, followed by anorexia and vomiting reported by eleven (50%) patients each. A history of raw milk ingestion (50%) was commonly seen. Cognitive impairment was the most common finding upon physical examination in 32% of the patients. Mostbut not all of the patients had elevated brucella titer in both CSF and blood while a few patients had positive blood and/or CSF cultures. One patient died acutely secondary to subarachnoid hemorrhage. The most common long-term complications seen were residual weakness and hearing loss in 23% and 9% respectively.

Conclusion:- Neurobrucellosis must be kept in mind when evaluating patients with non-specific neurological complaints especially in endemic areas. Early initiation and compliancewith anti-brucella treatment decrease the risk of developing complications.

Introduction:-

Brucellosis is a chronic granulomatous disease that has been successful in evading eradication by natural and medical means for thousands of years[1]. Brucellosis is caused by the different species of genus *Brucella* which are aerobic gram-negative intracellular coccobacilli[2]. Many species of brucella have been isolated. However, four species are well known to cause disease in human beings including *B.melitensis, B.suis*, *B.canis* and *B.abortus*.

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Brucellosistransmits to humans by direct inoculation through wound and abrasions, conjunctival contamination or inhalation of brucella-contaminated aerosols[3].However, the most common route of transmission is by the consumption of infected unpasteurized milk and milk products such as raw milk, cheese, and ice cream[4].

Brucella can virtually involve any system in the body including the central nervous system (CNS).The involvement of the CNShas been seen in 4-7% of the brucellosis patients reported in most of the studies [5-10]. Recently, a study has been conducted which provided the evidence that B.abortus and its lipoprotein activatesthe innate immunity of the CNS, eliciting an inflammatory response that leads to apoptosis of astrocytes (basic supporting cells of CNS) or astrogliosis. Hence, it is thought that the Brucella lipoprotein is the main virulence factor in the pathogenesis of neurobrucellosis.

Neurobrucellosis has a wide spectrum of signs and symptoms which can be categorized into central and peripheral forms[10]. The CNS involvement tends to be acute in nature and can be manifested as headache, meningitis, encephalitis, meningioencephalitis, myelitis as well as cerebellar dysfunction[10-12]. Peripheral neuropathy secondary to brucellosis could present with back pain, areflexia, paraplegia, paraparesis, or proximal nerve radiculopathy[10-11]. Other presentations of neurobrucellosis such as mycotic aneurysm, ischemic stroke and subarachnoid hemorrhage are not uncommon[11,12]. Other complications such as Guillian Barre syndrome[13], solitary posterior fossa abscess[14], diabetes insipidus[15]and central venous thrombosis[16]have been reported. Sincethe spectrum of the neurobrucellosis presentation is wide,it is not uncommon for it to be mixed with other neurological, neurosurgical or even psychiatric illnesses.

Establishing the diagnosis of brucella is challenging. The most definitive laboratory test is the isolation of bacterium from blood or tissue samples. However, cultures are positive in only 15-70% of the patients[17]. Other laboratory investigations include serum agglutination test and enzyme linked immunosorbent assays (ELISA) which are less specific but more sensitive than cultures[18]. One relatively new test that is more specific and sensitive is the polymerase chain reaction (PCR) of brucellaproteins [19-22].

The burden of brucellosis is significant worldwide with more than 500,000 casesannually and a prevalence of more than 10 cases per 100,000 population in some areas. This marks it as the most common zoonotic infection[23]. It is believed that brucellosis is hugely under diagnosed and under treated. Brucella is endemic in Saudi Arabia and countries boarding the Mediterranean Sea and other countries in the Middle East[24]. This is mostly secondary to the common practice of raw milk ingestion in these countries. The neurological involvement is an ominous sign resulting in increased morbidity and mortality of the disease. Although it is important to diagnose neurobrucellosis early to start prompt treatment and to limit complications, the diagnosis is delayed due to the nonspecific signs and symptoms resulting in increased risk of permanent neurological damage. The aim of our study is to show the broad clinical presentations, laboratory findings, complications and different outcomes of neurobrucellosis in our society.

Methodology:-

In a retrospective chart review study, we examined 517 patients confirmed to have brucellosis who presented to King Abdulaziz Medical City in Riyadh, Saudi Arabia, between the periods of 1995 to 2010. Out of those, 22 patients were found to have neurobrucellosis and were included in our study.

Neurobrucellosis was diagnosed using the following inclusion criteria:

1. A clinicalpicture suggestive ofneurobrucellosis such as headache, meningitis, encephalitis, meningioencephalitis, myelitis, cerebellar dysfunction, back pain, areflexia, paraplegia, paraparesis, proximal nerve radiculopathy as well as the systemic manifestations.
2. 2- Typical CSF changes such as pleocytosis (normal CSF cell count is 0-5 cells/mm^3), elevated CSF protein levels (normal level is 0.15-0.45 g/dl) and low CSF glucose levels (normal range is 60-85 mg/dl).
3. 3- Positive blood or CSF cultures for any of the brucella species.
4. 4- Positive serological tests (PCR, agglutination test titer more than or equal 1:160 in blood or 1:10 in CSF).

The presence of the first two points along with the third or fourth point is sufficient enough to include the patient in our study. All the patients fulfilled the required criteria except two, both of whom had CNS symptoms consistent with neurobrucellosis with positive blood serology and culture for brucella but refused to undergo lumbar puncture. However, when treated with anti-brucella medications, they recovered completely. The lack of other explanation for

their symptoms and the rapid response to anti-brucella medications encouraged us to presumptively consider them as neurobrucellosis and include them in our study.

Results:-

Out of the 517 patients presented to King Abdulaziz Medical City with neurobrucellosis between 1995-2010, twenty-two (4.25%) patients were found to have neurobrucellosis.Of those, eleven (50%) patients were males and eleven(50%) patients were females with an average age of 42.5 (range: 11-93 years). Sixteen patients (72.7%) presented mainly with neurologiccomplaints while another eight patients (36.4%) presented with a combination of neurologic and systemic complaints. Fourteen patients (63.7%) presented with systemic complaints with mild neurologic symptoms whiletwo patients (9.1%) had peripheral nervous system (PNS) related complaints.

The most common symptom seen in our cohort was fever in sixteen (73%) patients, followed by anorexia and vomiting reported by eleven (50%) patients each. Headache was reported by ten (45%) patients while easy fatigability and change in the level of consciousness were each reported in nine (41%) patients.

Table 1 demonstrates the presence of symptoms and their frequency in the neurobrucellosis patients in our study.

Table1: Summery of the symptoms seen in our patients

Symptoms	Frequency (%)
- Fever	16 (73%)
- Anorexia - Vomiting	11 (50%)
- Headache	10 (45%)
- Change in the level of consciousness - Easy Fatigability	9 (41%)
- Weakness	8 (36%)
- Chills - Low back pain	6 (27%)
- Arthralgia - Unsteady gait - Weight loss	5 (23%)
- Neck rigidity	4 (18%)
- Diarrhea - Hearing impairment - Night sweating	3 (14%)
- Aphasia - Cough - Dizziness - Visual disturbance	2 (9%)
- Abdominal pain - Behavioral changes - Photophobia - Seizure - Sensory changes - Urinary retention	1 (5%)

Only four (18%) patients were having one or more chronic diseases such as hypertension, diabetes mellitus (DM), or asthma, while the remaining eighteen patients(82%) were apparently healthy. Five (23%) patients had a history of a family member previously affected with brucellosis. Eleven (50%) patients had a history of raw milk ingestion while nine (41%) had a history of direct contact with animals namely camels.

On physical examination, eight (36%) patients were febrile, thirteen (59%) patients were tachycardiac and eight (36%) patients were tachypnic. Cognitive impairment was the most common neurologic finding, seen in seven (32%) patients. Other signs included neck stiffness in six (27%) patients and focal neurological deficit in five (23%) patients.

Table 2 summarizes the signs seen in neurobrucellosis patients and their frequencies.

Table 2: The findings on physical examination of 22 neurobrucellosis patients.

Physical Findings	Frequency (%)
- Cognitive impairment	7 (32%)
- Neck stiffness	6 (27%)
- Focal motor deficit	5 (23%)
- Abnormal extraoccular movement - Cerebellar Signs, Dysarthria - Memory Impairment	4 (18%)
- Arthritis - Lung crepitation	3 (14%)
- Decreased visual acuity - Kerning's sign	2 (9%)
- Aphasia, apraxia - Dysphagia - Hearing loss - Heart murmur - Hepatospleenomegaly - Papilledema - Nystagmus	1 (5%)

Laboratory workup showed that only two (9%) patients had leukocytosis, three (14%) had thrombocytopenia, seven (32%) patients had hyponatremia and 14 (64%) patients hadelevated liver enzymes. All patients except one (95%) had elevated brucella titer in serum. Lumbar puncture was done for all patients except two patients who refused it. Out of the 20 patients whom underwent lumbar puncture, seventeen (85%) had pleocytosis with lymphocytic predominance, nineteen (95%) patients had elevated CSF protein levels and 13 (65%) had low CSF glucose levels. Fifteen CSF samples were sent for serology and out of them, fourteen (93%) had high titer for brucella species.

Table 3 shows the serology pattern in blood and CSF of our patients.

Table 3: Serological pattern in blood and CSF of 22 patients with neurobrucellosis.

Brucella Titer in Serum	Frequency (%)
Negative	1 (5%)
1:160	2 (9%)
1:320	3 (14%)
1:640	6 (27%)
1:1280	3 (14%)
1:2560	2 (9%)
1:5120	2 (9%)
1:10240	2 (9%)
≥1:20480	1 (5%)
Brucella Titer in CSF	**Frequency (%)**
Negative	1 (5%)
1:10	2 (10%)
1:20	1 (5%)
1:40	2 (10%)
1:80	2 (10%)
1:160	2 (10%)
1:320	2 (10%)
≥1:640	3 (15%)

Microbiologically, five patients (23%) had positive blood cultures for brucella species while only four (18%) patients had positive CSF cultures. Nine patients had brain CT and/or MRI and out of them, eight (89%) patients had abnormal radiological findings.

Residual weakness was the most common short-term complication observed in five (23%) of our patients followed by hearing impairment and seizure seen in twopatients (9%) each.

Table 4 shows the complications observed in our patients.

Table 4:- Complications seen in neurobrucellosis patients.

Complication	Frequency (%)
Residual weakness	5 (23%)
Hearing impairment	2 (9%)
Seizure	2 (9%)
Ataxia	1 (5%)
Dementia	1 (5%)
Diplopia	1 (5%)
Dysarthria	1 (5%)
Persistent Headache	1 (5%)

The average hospital stay for our patients was 23 days (range: 4-120 days). One (5%) patient died two months after the initiation of treatment secondary to subarachnoid hemorrhage. The rest, 21 (95%) patients, recovered with 17 (77%) patients being fully independent, three (14%) patients were partially dependent and 2 (9%) were fully dependent. Six (27%) patients were readmitted againwith a relapse of their disease. Furthermore, 3 of these patients were readmitted for a third time with the same diagnosis.

Discussion:-

In this study, we reported a cohort of 22 patients who presented to our hospital with features of neurobrucellosis and described their clinical presentation, serological patterns and short-term complications. We reported that neurobrucellosis was a serious complication in a significant percentage (4.3%) of patients with brucellosis. This is consistent with the findings of other studies in the Middle East that concluded that neurobrucellosis affects 4-7% of patients with brucellosis[5-10].

In addition, we examined the clinical presentation of those patients with neurobrucellosis to evaluate for any recognized pattern. Non-specific symptoms such as fever, anorexia, vomiting, change in the level of consciousness and easy fatigability were the most commonly seen features. These findings are consistent with clinical observations and previous studies. This emphasizesthe importance of considering this diagnosis when evaluating patients with risk factors who present with these symptoms[25,26,27].

Chronic health conditions may play arole in altering the natural history of neurobrucellosis by influencingthe immune system [28]. However, most of our patients were healthy and only four (18%) of themreported one or more comorbidities. This issimilar to the prevalence of common chronic health conditions in our population, which does not support any role of these diseases in increasing the risk of developing neurobrucellosis. However, the small sample size of our cohort limits our ability to draw any firm conclusions.

Consumption of raw milk products is considered the most significant risk factor for contracting brucellosis. Although expected to be high, only eleven patients (50%) had a history of raw milk ingestion while nine (41%) patients had a history of direct contact with animals. These low percentagesof reported animal exposure may have been confounded by reporting and recall biases. This also highlights the fact that a negative exposure to raw milk or dairy products does not eliminate the possibility of neurobrucellosis as the underlying diagnosis.

Nonspecific laboratory findings,that may indicate end organ involvement, are commonly seen in neurobrucellosis patients. In our study, we reported seven patients (32%) with significant neutropenia which is a known complication of neurobrucellosis[29,30]. Liver involvement is also a relatively common finding in patients with

neurobrucellosis[23]. It seems that this is multifactorial in origin and could be developed after brucellosis infection or caused by anti-brucella medications injury[31,32].

Laboratory confirmation of neurobrucellosis is challenging because of the prolonged culture time. Blood and CSF cultures remain the gold standarddiagnostic tests to confirm neurobrucellosis infections despite their poor sensitivity [10,27,33]. For this reason, serological methods are more commonly used to diagnose neurobrucellosis. In our study, 95% of the patients had elevated brucella titers in their serum.

Neurobrucellosis is not a benign disease and even if treated early, those patients can develop serious complications. In this study, fivepatients (23%) had residual weakness while two patients (9%) ended with permanent hearing loss. These are two well-known complications of neurobrucellosis[34,35]. A similar study on 18 patients with neurobrucellosis reported similar frequencies of long term complications where 5 (28%) patients had residual neurological deficits and 4 (22%) developed permanent hearing loss[36].This highlightsthe importance of early detection and treatment of the disease as well as the importance of the long term follow up to evaluate the development of complications.

Our patients received different antibiotic combinations with different durations of therapy (5-44 weeks). Details of antimicrobial regimens received by our cohort can be found in the previously reported study[37]. The mortality rate of neurobrucellosis in our hospital is about 5%, which is similar to the rates reported byprevious studies[38,39].

In conclusion, it is clear that neurobrucellosis has nonspecific presenting signs and symptoms and it poses a challenge for establishing the diagnosis. The disease should be considered in the deferential diagnosis of patients with nonspecific neurological presentations especially in endemic areas. Compliance with medications presents a great challenge due to the long duration of treatment with multiple agents. It is thus crucial to educate all patients about the disease and its potential complications.

List of Abbreviations

- CNS: Central Nervous System
- ELISA: Enzyme Linked Immunosorbent Assay
- PCR: Polymerase Chain Reaction
- CSF: Cerebrospinal Fluid
- PNS: Peripheral Nervous System
- DM: Diabetes Mellitus
- CT: Computed Tomography
- MRI: Magnetic Resonance Imaging

Ethical Approval:-

This study was approved by the Institutional Review Board at King Abdulaziz Medical City in Riyadh, Saudi Arabia (#RR010/011).

Competing interest statement:-

We, the authors of this manuscript, confirm that none of us have any competing interest.

References:-

1. Capasso L. Bacteria in two-millennia-old cheese, and related epizoonoses in Roman populations.J Infect. 2002;45:122-7.
2. Godfroid J, Cloeckaert A, Liautard JP, Kohler S, Fretin D, Walravens K, Garin-Bastuji B, Letesson JJ. From the discovery of the Malta fever's agent to the discovery of a marine mammal reservoir, brucellosis has continuously been a re-emerging zoonosis. Vet. Res. 2005;36:313-26.
3. Ergönül Ö, Çelikbaş A, Tezeren D, Güvener E, Dokuzoğuz B. Analysis of risk factors for laboratory-acquired brucella infections. J Hosp Infect. 2004;56:223-7.
4. Young EJ.An overview of human brucellosis.Clin Infect Dis. 1995 ;21:283-9.
5. Ariza J, Pujol M, Valverde J, Nolla JM, Rufi G, Viladrich PF, Corredoira JM, Gudiol F. Brucellarsacroiliitis: findings in 63 episodes and current relevance. Clin Infect Dis. 1993;16:761-5.
6. Solera J, Lozano E, Martínez-Alfaro E, Espinosa A, Castillejos ML, Abad L. Brucellar spondylitis: review of 35 cases and literature survey. Clin Infect Dis.1999;29:1440-9.

7. Navarro-Martïnez A, Solera J, Corredoira J, Beato JL, Alfaro EM, Atiénzar M, Ariza J. Epididymoorchitis due to Brucella mellitensis: a retrospective study of 59 patients. Clin Infect Dis. 2001;33:2017-22.
8. Khan MY, Mah MW, MemishZA.Brucellosis in pregnant women.Clin Infect Dis. 2001;32:1172-7.
9. Ariza J, Pigrau C, Canas C, Marron A, Martinez F, Almirante B, Corredoira JM, Casanova A, Fabregat J, Pahissa A. Current understanding and management of chronic hepatosplenicsuppurative brucellosis. Clin Infect Dis. 2001 ;32:1024-33.
10. Shakir RA, Al-Din AS, Araj GF, Lulu AR, Mousa AR, Saadah MA. Clinical categories of neurobrucellosis. Brain. 1987;110:213-23.
11. McLean DR, Russell N, Khan MY. Neurobrucellosis: clinical and therapeutic features.Clin Infect Dis. 1992;15:582-90.
12. [Bouza E, de la Torre MG, Parras F, Guerrero A, Rodríguez-Créixems M, Gobernado J. Brucellar meningitis. Clin Infect Dis. 1987;9:810-22.
13. NNamiduru M, Karaoglan I, Yilmaz M. Guillain-Barre syndrome associated with acute neurobrucellosis.Int J ClinPract. 2003;57:919-20.
14. Solaroglu I, Okutan EK, Beskonakli E. Solitary extra-axial posterior fossa abscess due to neurobrucellosis. J ClinNeurosci. 2003;1:710-2.
15. Trifiletti RR, Restivo DA, Pavone P, Giuffrida S, Parano E. Diabetes insipidus in neurobrucellosis. ClinNeurolNeurosurg. 2000;102:163-5.
16. Zaidan R, Al Tahan AR. Cerebral venous thrombosis: a new manifestation of neurobrucellosis. Clin Infect Dis. 1999;28:399.
17. Memish Z, Mah MW, Al Mahmoud S, Al Shaalan M, Khan MY. Brucella bacteraemia: clinical and laboratory observations in 160 patients. J Infect. 2000;40:59-63.
18. Ariza J, Pellicer T, Pallares R, Foz A, Gudiol F. Specific antibody profile in human brucellosis. Clin Infect Dis. 1992;14:131-40.
19. Matar GM, Khneisser IA, Abdelnoor AM. Rapid laboratory confirmation of human brucellosis by PCR analysis of a target sequence on the 31-kilodalton Brucella antigen DNA. J ClinMicrobiol. 1996;34:477-8.
20. Redkar R, Rose S, Bricker B, DelVecchio V. Real-time detection of Brucella abortus, Brucella melitensis and Brucella suis. Mol Cell Probes. 2001;15:43-52.
21. Probert WS, Schrader KN, Khuong NY, Bystrom SL, Graves MH.Real-time multiplex PCR assay for detection of Brucella spp., B. abortus, and B. melitensis.JClinMicrobiol. 2004;42:1290-3.
22. Queipo-Ortuño MI, Colmenero JD, Baeza G, Morata P. Comparison between LightCycler Real-Time Polymerase Chain Reaction (PCR) assay with serum and PCR–enzyme-linked immunosorbent assay with whole blood samples for the diagnosis of human brucellosis. Clin Infect Dis. 2005;40:260-4.
23. Economou M, Pappas G. New global map of Crohn's disease: Genetic, environmental, and socioeconomic correlations. Inflamm Bowel Dis. 2008 ;14:709-20.
24. Bahemuka M, Shemena AR, Panayiotopoulos CP, Al-Aska AK, Obeid TA, Daif AK. Neurological syndromes of brucellosis.JNeurolNeurosurg Psychiatry. 1988;51:1017-21.
25. Shakir RA. Neurobrucellosis. Postgrad Med J. 1986;62:1077
26. Bodur H, Erbay A, Akinci E, C¸ olpan A, C¸ evik MA, Balaban N.Neurobrucellosis in an endemic area of brucellosis.Scand J Infect Dis. 2003;35:94-7.
27. Kochar DK, Agarwal N, Jain N, Sharma BV, Rastogi A, Meena CB. Clinical profile of neurobrucellosis--a report on 12 cases from Bikaner (north-west India). J Assoc Physicians India2000;48:376-80.
28. Yousif B, Nelson J. Neurobrucellosis–a rare complication of renal transplantation.Am J Nephrol. 2001;21:66-8.
29. Giordano S, Failla MC, Di Gangi M, Miceli S, Abbagnato L, Dones P. Thrombocytopenia associated with brucellosis: a case report].Infez Med. 2008;16:158-61.
30. Sari I, Altuntas F, Hacioglu S, Kocyigit I, Sevinc A, Sacar S, Deniz K, Alp E, Eser B, Yildiz O, Kaynar L. A multicenter retrospective study defining the clinical and hematological manifestations of brucellosis and pancytopenia in a large series: Hematological malignancies, the unusual cause of pancytopenia in patients with brucellosis. Am J Hematol 2008;83:334-9.
31. Onder C, Bengur T, Kirci A, Mine T, Zafer B, Belkis U, Kadir A, Gazi Y. Etiological role of brucellosis in autoimmune hepatitis. World J Gastroenterol. 2005;11:2200.
32. La Spada E, Micalizzi A, La Spada M, Quartarano P, Nugara G, Soresi M, Affronti M, Montalto G. [Abnormal liver function in brucellosis].Infez Med. 2008;16:148-53.
33. Baldi PC, Araj GF, Racaro GC, Wallach JC, Fossati CA. Detection of Antibodies to BrucellaCytoplasmic Proteins in the Cerebrospinal Fluid of Patients with Neurobrucellosis. Clin Vaccine Immunol. 1999;6:756-9.

34. Gul HC, Erdem H, Gorenek L, Ozdag MF, Kalpakci Y, Avci IY, Besirbellioglu BA, Eyigun CP. Management of neurobrucellosis: an assessment of 11 cases. Intern Med 2008;47:995-1001.
35. Ersöz-Arat M, Karsen H, Bakırcı A, Akdeniz H.A case of neurobrucellosis with coma. KlimikDerg. 2006;19:36-7.
36. McLean DR, Russell N, Khan MY. Neurobrucellosis: clinical and therapeutic features. Clin Infect Dis. 1992;15:582-90.
37. Alothman A, Al Dubayan S, Al Khathaami A, Kojan S, Salih SB. neurobrucellosis: challenges for Therapy. Infect Dis (Auckl). 2012;5:15.
38. MOUSA AR, KOSHY TS, ARAJ GF, MARAFIE AA, MUHTASEB SA, AL-MUDALLAL DS, BUSHARETULLA MS. Brucella meningitis: presentation, diagnosis and treatment-a prospective study of ten cases. QJM. 1986;60:873-85.
39. Ranjbar M, Rezaiee AA, Hashemi SH, Mehdipour S. Neurobrucellosis: report of a rare disease in 20 Iranian patients referred to a tertiary hospital. East Mediterr Health J 2009