Letter to the Editor

Dear Editor,

Cancer Screening and Anti-N-methyl-D-aspartate Receptor Encephalitis

The case of anti-N-methyl-D-aspartate (anti-NMDA) receptor encephalitis described by Ho et al is probably the third similar case reported from Hong Kong.[1] In contrast to the first two cases in whom ovarian teratomas were found, no apparent neoplastic disease was detected in their reported patient. The report touches on an interesting topic of cancer screening in paediatrics. It also raises the queries if the appropriate tests have been done for cancer screening and if malignancy can be excluded based on the reported findings.

In children under the age of 18 years who have been diagnosed with anti-NMDA receptor encephalitis, the risk of an underlying ovarian teratoma is 31%.[2] Thus, even though the incidence is much less than that of the adult patient, cancer screening is strongly justified in the reported patient.

Cancer detection in children involves the use of testing specific tumour markers in the blood or urine, diagnostic imaging, and opthalmological examination with or without general anaesthesia. The choice depends on the target cancer, potential harms and cost for the patient. Even though ovarian teratomas are the commonest malignancy observed in paediatric cases of anti-NMDA receptor encephalitis, other diagnoses such as Hodgkin lymphoma[3] and neuroblastoma[2] have been noted. Ultrasonography of the pelvis or testes has been recommended for detecting ovarian or testicular teratomas but this is obvious not sufficient for the screening of other malignancies. The use of positron emission tomorgraphy, coupled with computed tomorgraphy (CT) or magnetic resonance imaging, may be a better option for children with anti-NMDA encephalitis. In addition to the advantage of being a whole body scan, the use of ^{18}F-flurodeoxyglucose may be able to pick up focal areas of malignant transformation in otherwise benign-looking teratomas and provide a functional imaging of the central nervous system for the assessment of encephalitis.

In addition, measurement of serum α-fetoprotein and β-human chorionic gonadotropin may be a useful adjunct for the detection of immature teratomas. It is surprising that none of these tests was mentioned in the case report.

Repeated cancer screening is often recommended in patients with anti-NMDA receptor encephalitis as the neuropsychiatric manifestations may precede the occurrence of detectable cancer.[2] In extreme cases, the neoplastic origin can only be confirmed at oopherectomy. Johnson et al reported a 35-year-old woman who was refractory to treatment with intravenous immunoglobulin, rituximab and cyclophosphamide.[4] Despite repeated ultrasonography and CT, no malignancy was found. Five months into her illness. oopherectomy was carried out after which she made a good recovery. An occult teratoma was found. Boeck et al reported another case in a 34-year-old woman whose encephalitis was refractory to treatment with high-dose methylprednisolone, intravenous immunoglobulin, plasma exchange, rituximab and cyclophosphamide.[5] Repeated imaging and bilateral ovarian biopsies failed to identify any malignant disorder. At 11 months of presentation, an oopherectomy was performed which was followed by clinical improvement. A mature teratoma with partial neuronal differentiation was found. In both cases, the decision to go for the surgery was prompted by subtle abnormalities detected in one of the ovaries on repeated imaging and the lack of clinical improvement despite vigorous immunosuppressive treatment.

Ho et al's report is therefore an interesting case and the diagnosis and management of anti-NMDA receptor encephalitis remains challenging for paediatricians, especially for the neurologists and oncologists.

References

1. Ho KK, Yau EK, Yiu WL, Fong NC. Anti-N-methyl-D-aspartate receptor encephalitis: a potentially treatable cause of neuropsychiatric syndrome. HK J Paediatr(new series) 2013;18: 226-9.
2. Florance-Ryan N, Dalmau J. Update on anti-N-methyl-D-aspartate receptor encephalitis in children and adolescents. Curr Opin Pediatr 2010;22:739-44.
3. Lee AC, Ou Y, Lee WK, Wong YC. Paraneoplastic limbic encephalitis masquerading as chronic behavioural disturbance in an adolescent girl. Acta Paediatr 2003;92:506-9.
4. Johnson N, Henry C, Fessler AJ, Dalmau J. Anti-NMDA receptor encephalitis causing prolonged nonconvulsive status epilepticus. Neurology 2010;75:1480-2.
5. Boeck AL, Logemann F, Kraub T, et al. Ovarectomy despite negative imaging in anti-NMDA receptor encephalitis: effective even late. Case Rep Neurol Med 2013;2013:843192.

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