Acute reversible seronegative cerebellar ataxia in a young woman with ovarian teratoma

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Dear editor,

We report a case of a young woman with acute reversible cerebellar ataxia secondary to ovarian teratoma with no identifiable serum antibodies.

1.0 Case report

A 25-year-old Somali woman presented with acute ataxia, dysarthria, dizziness and blurred vision on standing, preceded by a week of epigastric pain and recurrent vomiting. The gastrointestinal symptoms were initially diagnosed as viral gastroenteritis. One month prior to the presentation, she had fever, headache and arthralgia lasting one week. Her past medical history included vitamin D deficiency, for which she was on vitamin D supplementation. She had a strong family history of autoimmunity. Her mother and maternal grandmother suffered from rheumatoid arthritis and one of her maternal aunts suffered from systemic lupus erythematosus. She denied taking any other supplements or recreational drug use. She did not consume alcohol, tobacco or marijuana. She migrated from Kenya but had no recent overseas travel. On examination, she had wide based ataxic gait with difficulty sitting unsupported. There was head titubation, saccadic overshoot on right gaze, and bilateral rebound of upper limbs. Appendicular dysmetria and dysdiadochokinesia were evident on testing. Reflexes were brisk but equal throughout. She did not have any weakness or sensory deficits. Hoffman's sign was negative and plantar response was down-going.

Investigations showed mild lymphocytosis in the cerebrospinal fluid (CSF) and positive oligoclonal bands. Paraneoplastic antibodies including anti-Hu, Yo, Ri, amphiphysin, CRPM5, Ma1/2, Tr, N-methyl-D-aspartate [NMDA] receptor and GAD-65 antibodies were negative. Autoimmune screen including ANA, ENA, dsDNA were normal. Further laboratory results are detailed in supplemental Table 1. Brain magnetic resonance imaging (MRI) was within normal limits. Computed tomography of the chest and abdomen revealed a partially fatty and partially calcified ovoid mass in the left adnexa measuring 25mm and peribronchial ground glass infiltrate in the left apex of the lung. Pelvic ultrasound confirmed features consistent with left ovarian dermoid cyst. Breast ultrasound did not show any suspicious lesions.

The patient had ongoing nausea, vomiting and worsening ataxia. The gynaecology team did not feel that the dermoid cyst was relevant to the patient's presentation. Gastroscopy and bronchoscopy were therefore performed and were normal. Positron emission tomography (PET) showed a moderately fludeoxyglucose(FDG)-avid left ovarian lesion. Due to concerns of malignant transformation, a left oophorectomy was performed one month into the admission. Histopathology demonstrated a mature teratoma with aggregates of reactive lymphoid cells around the neural tissue (Figure 1). We treated her with intravenous methylprednisolone and intravenous immunoglobulin subsequent to the oophorectomy. The patient improved rapidly over two weeks and returned to almost baseline function by six months, with no recurrence of symptoms at one-year.

2.0 Discussion

Ovarian tumours are associated with paraneoplastic cerebellar degeneration, opsoclonus-ataxia syndrome(1) and anti-NMDAR encephalitis(2). Teratomas are the most common ovarian tumours below the age of 30 but the exact prevalence is unknown(3). Although they are often asymptomatic with low potential for malignant transformation, this case illustrates that teratomas can cause a sero-negative acute ataxic syndrome. Increased FDG-PET uptake

in this case potentially reflects an inflammatory process and corresponds with inflammatory infiltrates within the teratoma. This lends support to the diagnosis of neurological paraneoplastic phenomenon. In a recent case series of 249 patients with teratoma-associated encephalitis, 22 antibody-negative patients developed a brainstem-cerebellar syndrome(4). Three quarters of them fully recovered after tumour resection and immunotherapy. We postulate that there is cross-presentation of an unidentified antigen on both the teratoma and cerebellar Purkinje cells, with an unknown precipitant such as a viral infection. Neurologists should consider ovarian teratoma as a potential reversible paraneoplastic syndrome in a young woman presenting with acute ataxia.

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Blood tests					
Hb	144g/L	ANA	2U/nL	Hu (ANNA-1)	Negative
WCC	5×10*9/L	ENA	Negative	Yo (PCA1)	Negative
Plt	428×10*9/L	ANCA	<2units	Ri (ANNA-2)	Negative
Bili	<2μmol/L	dsDNA	<1U/mL	Amphiphysin	Negative
ALT	9U/L	ACE	48U/L	CV2 (CRPM5)	Negative
Na	137mmol/L	RhF	<10kU/L	Ma1/2	Negative
K	3.6mmol/L	tTg IgA	<1U/mL	NMDAR	Negative
Ca	2.37mmol/L	C3	1.13g/L	Tr (PCA2)	Negative
BUN	2.1mmol/L	C4	0.3g/L	GAD-65	0.2
Crea	44μmol/L	Vit E	25μmol/L	AQP4	0
CRP	<1.0mg/L	Folate	39.9nmol/L	Ganglioside antibodies	Negative
ESR	16mm/hr	Vit B12	790pmol/L		
TSH	3.8 mU/L	bHCG	<1U/L		
TPO	<1kU/L	HIV serology	Negative		

Cerebral spinal fluid	
Gross appearance	Colourless
Opening pressure	14cmH2O
Leucocyte	5×10*6/L
Erythrocyte	35×10*6/L
Protein	0.4
Glucose	2.6mmol/L
Oligoclonal bands	Positive
NMDAR	Negative
GAD-65	Negative
Herpes virus PCR	Negative
Cytology	Mild lymphocytosis
Flow Cytometry	No monoclonal B cell or aberrant T cell population
Crytococcal antigen	Negative
Protein 14-3-3	Negative

Table 1. Laboratory tests

Hb, haemoglobin; WBC, white cell count; Plt, platelet count; Bili, bilirubin; ALT, alanine aminotransferase; Na, sodium; K, potassium; Ca, calcium; BUN, blood urea nitrogen; Crea, creatinine; CRP, C-reactive protein; ESR, erythroycyte sedimentation rate; TSH, thyroid stimulating hormone; TPO, thyroid peroxidase antibodies; ANA, antinuclear antibodies; ENA, extractable nuclear antigens; ANCA, anti-neutrophil cytoplasmic antibodies; dsDNA, double standed deoxyribonucleic acid antibodies; ACE, angiotensin converting enzyme; RhF, rheumatoid factor; ttG IgA, tissue transglutaminase antibodies immunoglobulin A; C3/4, complement ¾; vit, vitamin, bHCG, beta human chorionic gonadotropin; HIV, human immunodeficiency virus; NMDAR, N-methyl-D-aspartate receptor; GAD-65, glutamic acid decarboxylase 65 antibodies; PCR, polymerase chain reaction.

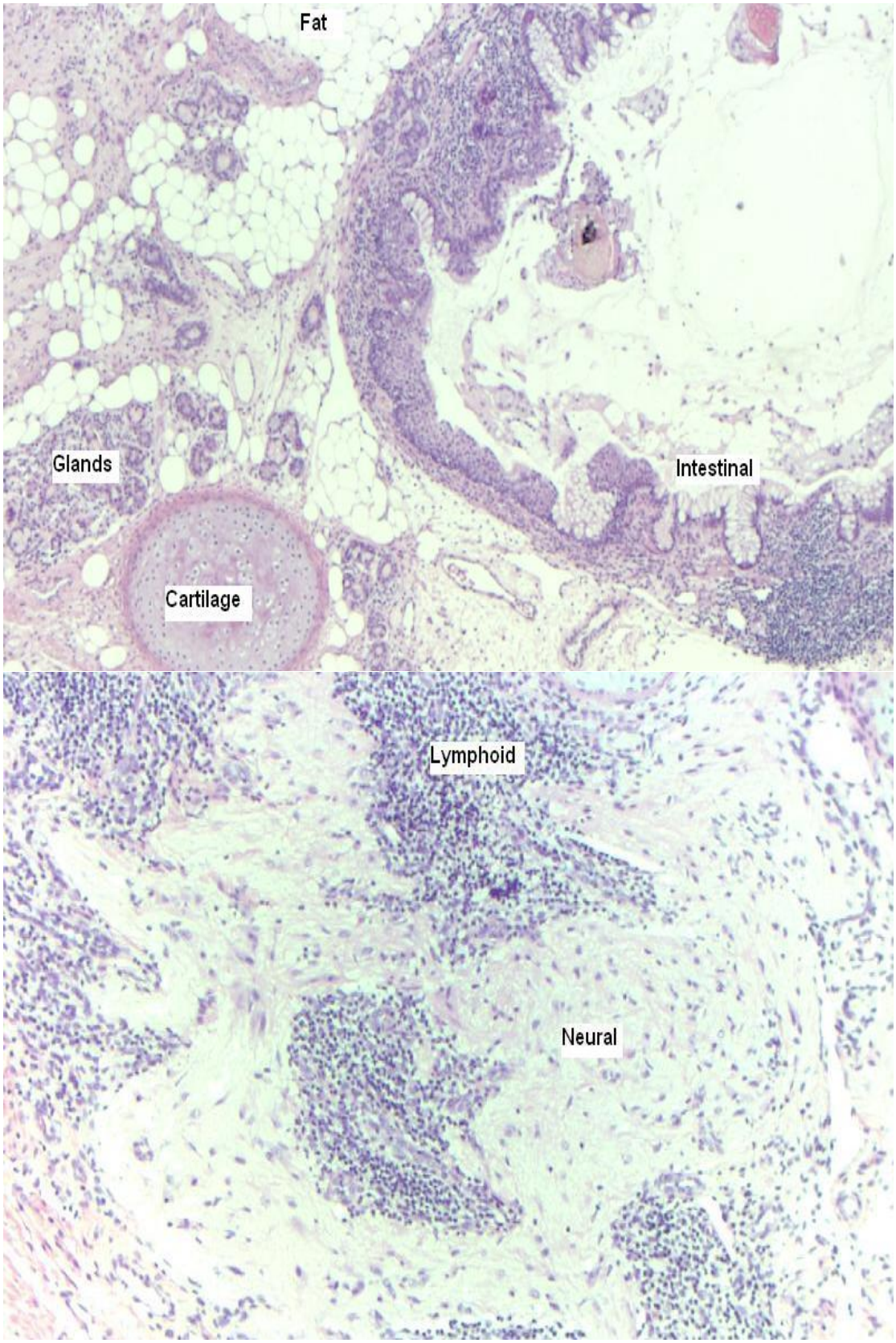

Figure 1. The upper panel shows an overview of part of the teratoma with hematoxylin and eosin stain. There are tissue from all three embryological layers. These include intestinal and glands from endoderm, cartilage and fat from mesoderm and neural glial

tissue from ectoderm. All tissue is mature. The lower panel showes a high power view (magnification by 100) of neural tissue composed of spindle cells in a fibrillary background and neuronal cells, adjacent to aggregates of reactive lymphoid cells. Courtesy of Dr Ebo Oost PathWest Laboratory Medicine Western Australia, King Edward Memorial Hospital.