observed. Here, we report a case of NMZL with a granulocytoid appearance of nuclei and a Pelger–Huët-like anomaly in a peripheral blood smear.

A 56-year-old female presented with neck lymphadenopathy and night sweats for 4 months. Her complete blood count demonstrated haemoglobin 88 g/L, lymphocytes $22.73 \times 10^9/L$ and platelets $156 \times 10^9/L$. The blood film revealed 78% abnormal lymphocytes, which mimicked granulocytic development in nuclear morphology, including metamyelocyte-like kidney bean-shaped nuclei (Fig. 1A–D), band-shaped nuclei (Fig. 1E–H) and multilobed nuclei (Fig. 1I–L). It was interesting to note that some neoplastic lymphocytes showed pseudo Pelger–Huët-like pince-nez-shaped nuclei (Fig. 1M–P). Flow cytometric analysis performed on bone marrow revealed the presence of an atypical lymphocyte population that comprised 83% of the total lymphocytes analysed. The atypical lymphocytes expressed CD19, CD22, lambda, and CD200 and partially expressed CD23 but lacked CD5, CD10, CD103, kappa, CD138, CD38, CD34, and sIgM. Molecular study revealed *BIRC3* and *P53* mutations. Bone marrow and lymph node biopsies confirmed the diagnosis of NMZL with bone marrow infiltration.

Pelger–Huët anomaly is an inherited benign condition that is characterised by the abnormality of chromosome segregation of neutrophils leading to bilobed, peanut- or dumbbell-shaped nuclei. The classic morphological abnormality is known to be caused by mutations of the Lamin B receptor (LBR) gene, which maintains the nuclear membrane structure.⁴ Pseudo Pelger–Huët anomaly, as a marker of granulocytic dysplasia, is only involved in neutrophils, which may occur in myelodysplastic syndrome (MDS) and acute and chronic leukaemias or can be drug-induced.^{5,6} The Pelger–Huët-like anomaly of lymphocytes is an extremely uncommon phenomenon that, to the best of our knowledge, has not been reported before. In contrast to the neutrophil Pelger–Huët anomaly, which is caused by failure of nuclear segmentation, the lymphocyte Pelger–Huët-like anomaly is caused by abnormal nuclear lobulation.

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Micronodular thymoma with lymphoid stroma: a clinicopathological study of five cases

Sir,

Micronodular thymoma with lymphoid stroma (MTLS) is a rare subtype of thymoma that was a new inclusion in the third edition of the World Health Organization (WHO) Classification of Tumours of the Lungs, Pleura, Thymus and Heart released in 2004.¹ Recognition of this histological subtype of thymoma is important as it has an excellent prognosis, with only a single published case of recurrence that occurred after incomplete initial resection.²

We identified all MTLS from the archives of Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital, NSW Health Pathology, Sydney, and reviewed clinical and pathological features. Over an 8-year time period, five cases of MTLS were identified.

The patients were four women and one man, aged between 58 and 70 years (mean 65.4 years) (Table 1). All tumours were found incidentally on computed tomography within the thymus in the anterior mediastinum and there was no evidence of regional nor metastatic spread. None of the patients had symptoms consistent with myasthenia gravis or any other autoimmune diseases. All patients underwent thymectomy, one with a minimally invasive surgical technique with the rest via conventional midline sternotomy. Two patients had cardiac valve pathology requiring intervention, which was attended to at the same time as thymectomy.

Tumour size ranged between 22 and 60 mm in maximum dimension (mean 45.4 mm). One tumour was solid, with the rest mixed solid and cystic. There were similar histological findings in all tumours (Fig. 1A–D). The tumours were well circumscribed and one tumour had a variable thickness capsule, with the rest unencapsulated. There were coalescing nests of bland oval to elongated epithelial cells with an intervening rich lymphoid stroma. The epithelial cells showed oval vesicular nuclei, small nucleoli and moderate amounts of indistinct pale eosinophilic cytoplasm. The lymphoid stroma contained follicles with reactive germinal centres. Up to four lymph nodes were identified within the

Table 1 Clinical features of five patients with micronodular thymoma with lymphoid stroma

Case	Patient factors						Tumour factors		
	Age	Sex	Presentation	MG	Site	Operation	Size, mm	Solid/cystic	Capsule
1	70	F	Incidental finding on workup for dyspnoea	No	Thymus	Sternotomy and thymectomy	50×40×35	Mixed	Variable thickness capsule
2	58	F	Incidental finding	No	Thymus	Sternotomy and thymectomy	35×34×20	Mixed	Unencapsulated
3	70	F	Incidental finding on workup for mitral valve surgery	No	Thymus	Redo sternotomy, bioprosthetic mitral valve replacement, thymectomy	60×30×20	Solid	Unencapsulated
4	65	M	Incidental finding on work up for unrelated soft tissue mass	No	Thymus	Robotic-assisted thoracoscopic thymectomy	60×58×34	Mixed	Unencapsulated
5	64	F	Incidental finding on work up for aortic valve surgery	No	Thymus	Sternotomy, bioprosthetic aortic valve replacement and thymectomy	22×20×20	Mixed	Unencapsulated

F, female; M, male; MG, myasthenia gravis.

main or accompanying specimens, all of which were free of tumour and showed reactive changes only. Three tumours were stage II and two tumours were stage I by Modified Masaoka staging. All cases were American Joint Committee on Cancer (AJCC) eighth edition T1aN0M0 stage group I. All tumours were completely excised (R0).

Immunohistochemical studies showed the epithelial component consistently stained positively for cytokeratins and PAX8 and occasional CD117 cell positivity (Fig. 2). The lymphoid component included CD20+ B cells within the follicles and CD3+ T cells mostly in the interfollicular areas. The germinal centres contained CD10+/BCL2– B cells in keeping with reactive follicles. CD5 stained T cells only.

Small numbers of immature TdT+/CD1a+ T cells were seen in close association with the epithelial component only.

Patients were discharged home between day one and day 19 following surgery. Delays to discharge were not due directly to the thymectomy. Follow-up was between one month and eight years with no tumour recurrences or metastases.

Micronodular thymoma with lymphoid stroma is a rare subtype of thymoma that was originally described by Suster and Moran in 1999.³ The largest prospective database, by the International Thymic Malignancy Interest Group (ITMIG), reported an incidence of MTLs of 1.4% of thymomas⁴ but these data were collected between 1983 and 2012, a time

Fig. 1 (A,B) Low power view of micronodular thymoma with lymphoid stroma showing coalescing nests of bland oval to elongated epithelial cells with an intervening rich lymphoid stroma. (C) Higher power view of epithelial nests. (D) Higher power view of reactive lymphoid follicles.

Fig. 2 (A) Low power view of CKAE1/3 showing positively staining epithelial elements. (B) Immature TdT+ T cells are closely associated with the epithelial elements. (C) CD20+ B cells are mostly confined to follicles. (D) CD3+ T cells are mostly seen in the interfollicular areas.

predominantly prior to the inclusion of the entity in the WHO Classification of tumours. A much smaller but more recent collection of data reported an incidence of 3.7%.⁵

Rarely, MTLs may occur in association with thymic follicular hyperplasia⁶ and other classical WHO subtypes of thymoma.⁷ Also recognised is the span of differentiation from MTLs to its malignant counterpart, thymic carcinoma with lymphoid stroma, with the most important malignant criteria including the marked cytological atypia, mitotic rate and Ki-67 index, the presence of CD5+ tumour cells and a lack of TdT+ T cells within the tumour.⁸ Early literature includes cases of MTLs that by more recent definitions would be classified as thymic carcinoma with lymphoid stroma, and therefore likely skew analysis of MTLs with regards to prognosis. Our cases showed no significant aberration from the classically described MTLs and no features concerning for malignancy.

With regards to clinical factors, our patients had a mean age of 65.4 years, similar to the mean age of 64.5 years reported in the WHO Classification but younger than the mean of 74 years reported by Szolkowska *et al.*^{1,5} Previously reported slight male predominance was not seen in our cases where four of five were females.¹ Consistent across the literature and our cases is the tendency for tumours to present as incidental findings. All of our cases were sited within the thymus in the anterior mediastinum and only very rare cases have been reported in the neck.⁹ None of our cases had symptoms of myasthenia gravis compared to 3.4% in the review by Liu *et al.*¹⁰

Tumour factors also were predominantly consistent between the reported literature and our cases including tumour size (our cases were 22–60 mm compared with 12–107 mm in Liu *et al.*)¹⁰ and the variable presence of cystic areas. In the

literature, cases spanned all Masaoka stages I–IV¹⁰ with a predominance of stages I and II. The ITMIG data found that 96% of MTLs were within these early stages,⁴ as were all of our cases.

Histologically, the tumours have a distinctive appearance with separate foci of epithelial tumour cells in small solid nests or cords with an abundant intervening lymphoid stroma that typically contains reactive lymphoid follicles (that may or may not contain germinal centres), along with possible plasma cells.¹⁰

Immunohistochemistry of MTLs, especially within the lymphoid component, showed some variability within the literature particularly in earlier reports but within our cases the findings were remarkably consistent. Similar to the original description of the entity by Suster and Moran,³ the lymphoid component in our cases were predominantly mature B cells with smaller numbers of immature T cells in the vicinity of the epithelial elements. Other cases in the literature have described some variations in the proportions of mature and immature T cells, and a lesser number of mature B cells, although some of these cases may not fulfil WHO criteria for MTLs diagnosis.^{11,12} Early concerns about MTLs promoting the development of mucosa-associated lymphoid tissue (MALT) lymphoma due to the expression of abnormal chemokines leading to this monoclonal B cell proliferation appears not to have eventuated.¹²

Unlike other more typical thymomas with a lymphoid stroma, most of the lymphoid cells are not intimately interspersed with the epithelial cells, they are predominantly B cells rather than immature T cells, and there is lymphoid follicle formation. As such, distinction from other more conventional thymoma subtypes can be made on morphological and immunohistochemical grounds. An important

differential diagnosis is thymic MALT lymphoma that is also characterised by a lymphoid proliferation with reactive follicles and interspersed epithelial elements. Unlike MTLs, MALT lymphomas lack solid nodules of neoplastic epithelial cells, and they exhibit lymphoepithelial lesions and a monoclonal B-cell proliferation that can readily be demonstrated by immunohistochemistry for light chain restriction in the plasma cell component. In reactive thymic follicular hyperplasia, the normal thymic architecture and Hassall's corpuscles are retained and there is a strong association with myasthenia gravis.

Our cases all presented with early stage disease and have so far followed the international literature experience of extremely low rates of disease specific morbidity and mortality with no recurrences.

In conclusion, we present five cases of MTLs, a rare subtype of thymoma with striking morphology that is distinct from other more common thymoma subtypes. Recognition of this uncommon entity is important to avoid confusion with reactive or neoplastic lymphoid proliferations or other thymic epithelial tumours. The combination of the classical architecture of multiple discrete small nests of bland oval epithelial cells amongst the dense lymphoid component with follicle formation is striking, and the recognition of TdT+ immature T cells within the vicinity of the epithelial component is specific.

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EGFR mutation profile in Australian patients with non-small cell lung cancer

Sir,

In Australia, funded access to tyrosine kinase inhibitors (TKIs) is limited to those patients with non-squamous or not otherwise specified (NOS) non-small cell lung cancer (NSCLC) who have an activating *EGFR* gene mutation. Given the requirement for *EGFR* testing for access to reimbursed TKIs, the TARget *EGFR* Access Program was established and ran between 2012–2014 and has provided data about the frequency of *EGFR* mutations in the Australian population.

Mutations in the *EGFR* gene were detected in 707 patients using Cobas V1 (Roche Molecular Diagnostics, Australia) ($n=794$, 46.5%) or Sanger sequencing ($n=913$, 53.3%). Cobas identifies 41 *EGFR* mutations, including *T790M* with at least 5% mutant alleles. Sanger sequencing can detect all mutations within the *EGFR* gene¹ with a tumour cell content of at least 10%.

The following were involved in the program: Peter MacCallum Cancer Centre, Melbourne; SydPath Pathology, Sydney; Sullivan Nicolaides Pathology, Brisbane; PathWest, Perth; and Austin Pathology, Melbourne. Sample characteristics are provided in Table 1. Data on referrer, sample type, tumour cell content, macro-dissection, turnaround time for sample, testing methodology, the test result and the turnaround time for clinical reporting and additional patient demographic information including age, gender and postcode of the patient, were collected.

Patients were referred for testing by their oncologist ($n=842$, 49.3%), pathologists ($n=554$, 32%) and clinicians ($n=192$, 11%). The demographics of our cohort were representative of the Victorian Cancer Registry (VCR) Lung Cancer Cases 2011. No major differences were observed in sex or between rural and metropolitan demographics. While the majority of samples were biopsies ($n=1063$, 62.3%), there was a strong linear trend for more cell cytology cell blocks in areas from higher socioeconomic status, and proportionally more biopsies from lower socioeconomic areas and from