LETTER TO THE EDITOR

Author's response

Our recent review¹ on a cohort of fine needle aspiration of the breast reported an atypical rate of about 7%, and of these, about 2% had a histological follow-up. A further analysis was carried out on these cases with excision, yielding a benign rate of about 67%. Cases without histological excision were excluded from the calculation, as a significant number of cases were lost to follow-up, and while a proportion may not have been subjected to surgery because of radiological benignity, we cannot assume that these represent the majority. This figure was actually in concordance with that reported in the literature that ranges from 48% to 68%.^{2–5} Nevertheless, we concede that our reported benign rate of 67% taking into account only those with histological excision will represent a lower end of the range of benign outcomes of atypical aspirates.

The aim of our review was to evaluate cytological parameters predictive of excision outcome in a cohort of atypical aspirates. We did not set out to assess the accuracy of how an atypical diagnosis was made in cytology, and hence did not reclassify these atypical FNACs in this cohort. We agree that reclassification of specific criteria for diagnosis of atypia in breast aspirates will be a worthwhile exercise in further understanding and promoting precision in this category.

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CORRESPONDENCE

Hyaline vascular Castleman disease relapsing as T cell rich B cell lymphoma with paraneoplastic pemphigus

A 32-year-old woman presented with mild fever and solitary discrete cervical lymph node (5 cm) for 2 years. The excision biopsy showed preserved lymph-node architecture with prominent onion skinning (figure 1) and hyalinised blood vessels in the germinal centres (figure 1, inset). The patient was investigated thoroughly for lymph nodes elsewhere, but no lymph nodes could be detected. The overall picture was suggestive of localised Castleman disease (LCD), hyaline vascular type. The HIV, HHV-8 and Epstein Barr Virus serology was negative.

The patient returned 5 years later with abdominal distension, weight loss, cervical and inguinal lymphadenopathy, hepatosplenomegaly and vesicobullous skin rashes for 3 months. CT and MRI revealed multiple cervical, retroperitoneal and mediastinal lymph nodes (figure 2).

Lymph-node biopsy showed complete effacement of architecture and infiltration of subcapsular sinus by large and small lymphoid cells (figure 3). On immunohistochemistry, the larger cells were CD 19 positive, while the smaller ones were positive for CD 45 RO (figure 3, inset). CD 30 and CD 15 were negative. Thus, a diagnosis of T cell rich B cell

Figure 1 Hyaline vascular Castleman disease with prominent onion skinning and hyalinised blood vessels (H&E staining, 100×; inset: 400×).

Figure 2 CT abdomen and MRI neck (inset) showing enlarged lymph nodes.

lymphoma was made. The skin and mucosal biopsy showed the presence of intraepidermal bullous lesion with granular deposition of C3 at the basement membrane and IgG at the intercellular space in the epidermis on immunofluorescence examination suggestive of pemphigus (figure 4).

Thus, a final diagnosis of a LCD relapsing as disseminated T cell rich B cell lymphoma with paraneoplastic pemphigus was made.

The patient was started on CHOP regimen and is well 2 years postchemotherapy.

CD is a heterogeneous disease that displays varied clinical manifestations. Malignancy in association with Castleman disease (CD) has been described previously.^{1,2} Development of Hodgkin's disease is well known and is more often associated with PC type CD.^{3,4}

Non-Hodgkin's lymphomas (NHL) are more often associated with multicentric Castleman disease (MCD) than LCD with an incidence as high as 18% of MCD cases.¹ The diagnosis of MCD-NHL can be concurrent or occurs within 2 years of the initial detection, while that of LCD-NHL is stated to be 45.6 months (0–156).⁵ B-NHL is the predominant type in both forms.

The present case adds a new case to the literature and supports the existing data on LCD regarding the age of presentation, which was 32 years in the present case, and its localisation to neck region. HIV and HHV 8 serology was negative in our case, and histopathology showed features of the hyaline vascular subtype. Its development into B cell NHL also corroborates well with the literature. However, the present case is unique in that T cell rich B cell immunophenotype has not been reported previously in a setting of LCD. This case also showed an interesting finding of coexisting Para neoplastic Pemphigus which is known to occur with NHL as well as Castleman disease.

NHL associated with CD is usually high grade and presents at stage III or IV at diagnosis, as in this case. Therefore, it has an aggressive clinical course and poor prognosis.⁵ Combination chemotherapy such as cyclophosphamide, vincristine and

Figure 3 T cell rich B cell non-Hodgkin's lymphoma (H&E staining, 400 $\times$; inset: immunohistochemistry with Avidin-Biotin method and DAB as chromogen, 400 $\times$) T cell: CD 45 RO, B cell: CD 19.

Figure 4 Paraneoplastic pemphigus (H&E staining, 400 $\times$).

Take-home message

Owing to the preneoplastic potential in the hyaline vascular type, simple excision of the affected lymph node may not be sufficient in localised Castleman disease.

prednisone regimens, or Cyclophosphamide, Hydroxydaunorubicin, Oncovin and Prednisone regimens for treatment of Non Hodgkin's Lymphoma regimens, has an established role in CD-NHL treatment.

Thus, CD is a rare condition with an obscure pathogenesis. With preneoplastic potential in the hyaline vascular type, simple excision of affected lymph node may not be sufficient in LCD.

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Atypia in fine needle aspirates of breast lesions

The paper by Tran *et al* on the histological correlates of atypia in fine needle aspirates (FNAs) of the breast was useful in suggesting which cytological features are likely to indicate malignancy.¹ However, their conclusion that 67% of atypical FNAs are from benign lesions and 33% malignant tumours may be misleading.

In their review of 5340 cases, 363 (7%) of breast FNAs were diagnosed as atypical, but the authors include in their analysis only those 98 atypical aspirates that had a histological follow-up. The reason why the remaining 265 lesions were not biopsied was probably because, in most cases, they were clinically and radiologically benign; omitting these cases from analysis therefore constitutes a significant workup (verification) bias.² The true proportion of atypical FNAs that were from benign lesions is therefore likely to be significantly higher than their figure of 67% suggests, and a review of these patients' medical records would allow a fairly accurate estimate of the true figure. Including all 363 atypical FNAs in their analysis would also, by increasing the size of the cohort, address one of the criticisms of the study made by the authors themselves, thereby increasing the accuracy of the results by narrowing their CIs.

Furthermore, given that the assessment of cytological atypia is subjective, it is also rather surprising that none of the 98 aspirates originally reported as atypical was changed to either benign or malignant on review. This suggests that a further bias, namely review bias, may be present, as these FNAs were not subject to blinded review (by being mixed in with an unknown number of benign and malignant aspirates, for example). Knowing that all the FNAs reviewed had already been considered atypical might have unconsciously biased the reviewers in their interpretation of the cytological characteristics.

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