Figure 2 Sequencing of the *PRF1* gene with genomic DNA extracted from the bone marrow mononuclear cells from the patient at presentation shows heterozygous point mutation at 1168 C>T(Arg390stop) in the upper panel (A), while the other allele at the lower panel is normal (B).

FHL with specific underlying molecular alterations: FHL1 (unidentified gene located at 9q21–22), FHL2 (*PRF1* at 10q21), FHL3 (*UNC13D* at 17q25), and FHL4 (*STX11* at 6q24).⁴ In the majority of FHL2 cases, *PRF1* abnormality has been identified as homozygous mutations or as compound heterozygous mutations, with exceptional cases showing a single allele heterozygous mutation as in our patient.^{5,6} The *PRF1* mutation at 1168 C>T (Arg390stop) was previously identified in a Japanese FHL patient, who had another mutation of 1090–1091delCT as a compound heterozygous mutation (IU and SI, unpublished observations). The psychomotor retardation with cerebral palsy, epilepsy, and neuropathy at autopsy suggests that our patient might be a victim of FHL, which carries a high incidence of CNS lesions.⁷ Furthermore, immunohistochemical staining confirmed the defect in the expression of perforin by cytotoxic T cells. The alternative explanation is that her CHP is a new form of the heterozygous *PRF1* mutation-related haematological disorders such as lymphoma, leukaemia, and aplastic anaemia.^{8–10} It would be interesting to study *PRF1* mutations in patients with CHP and SPTL in the future, ideally including perforin expression and functional cytotoxic T lymphocyte assays.

Previously, Craig *et al* found that some SPTL appear to EBV-associated, with malignant histopathology, and with terminal dissemination in a rapidly fatal progression.¹¹ However, classic CHP without proven lymphoma may be EBV-unrelated, with benign histology, and an indolent course unless developing terminal HLH. In our patient, the polyclonal EBV-negative T-cells without aberrant antigen loss and absence of lymphoma at autopsy indicate that she had a benign, classic CHP with fatal HLH rather than SPTL. Classical, benign CHP is a non-neoplastic disorder, yet this disease is usually fatal due to HLH and coagulopathy. We chose to use 13-cis-retinoic acid in this patient as it has been effective in patients with cutaneous lymphomas other than mycosis fungoides.¹² However, this agent offered only a transient response in our patient. Since the

distinction of CHP from SPTL is difficult and CHP might be a precursor of SPTL, Wick and Patterson suggested using the term “panniculitis-like subcutaneous lymphoma with cytophagocytosis” instead of CHP if strict clinicopathological criteria have been met, even without documented T-cell monoclonality.¹³ This approach would have a beneficial effect on treatment planning towards oncological rather than anti-inflammatory therapy. In line with that suggestion, Pettersson *et al* reported that three of their four CHP patients responded to immunosuppressive or cytostatic drugs.¹⁴ Considering the aggressive/refractory disease, part of which might be related to her *PRF1* mutation, our patient might have benefited from high-dose chemotherapy followed by autologous peripheral blood stem cell transplantation as suggested for the treatment of aggressive CHP.¹⁵

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Hamazaki-Wesenberg bodies in two patients with no history of sarcoidosis

Patient A

A 76-year-old woman underwent a left nephrectomy for a retroperitoneal angiomyolipoma, which was contacting and displacing the spleen and left kidney. Intraoperative frozen sections of a periportal lymph node revealed brown pigment within the sinuses. Permanent sections of this specimen demonstrated a reactive lymph node with lipogranuloma formation, prominent histiocytes, and ovoid, dark-brown to yellow structures located within the sinuses, associated with the prominent histiocytes. These structures ranged from 0.25–1.0 times the size of a lymphocyte nucleus and were primarily extracellular, with only occasional examples noted within histiocytes.

Patient B

A 55-year-old man underwent a right hemicolectomy for a tubulovillous adenoma of the ascending colon. Preoperative CT scan revealed

Figure 1 (A) H&E stained section at 60× magnification demonstrating numerous, variably sized, yellow-brown structures associated with histiocytes within the subcapsular sinus. Multiple bodies in close proximity can simulate budding yeast (arrow). (B) Fontana-Masson silver (FMS) stain emphasises the Hamazaki-Wesenberg bodies, colouring them black, though there can be artifact from debris associated with this stain. (C) Gomori methenamine Silver (GMS) likewise accents these bodies, darkly staining them against a green background. (D) Periodic acid-Schiff with an amylase digest (PAS-D) highlights the bodies, imparting on them a bright red colour.

mildly enlarged retroperitoneal lymphadenopathy, but no other evidence of metastasis. Eleven lymph nodes were located within the pericolic adipose tissue of the specimen, all negative for malignancy. Three of the eleven nodes demonstrated ovoid, dark-brown structures within the subcapsular sinuses, as well as lipogranuloma formation in one node. As in case 1, these structures were 0.25–1.0 times the size of a lymphocyte nucleus and were primarily extracellular, associated with histiocytes within the subcapsular sinuses.

Discussion

Hamazaki-Wesenberg bodies (alternatively termed yellow-brown bodies, yellow bodies, Hamazaki corpuscles) are structures of unknown significance, which have been periodically documented in the sinuses of lymph nodes in numerous anatomic locations and myriad medical conditions, including appendicitis, cirrhosis, lymphoid tumours, colon carcinoma and numerous others, most famously sarcoidosis.^{1–6} Initially described by Hamazaki in 1938 in mesenteric lymph nodes,⁶ and later noted by Menne in 1952 in 70% of mesenteric lymph nodes removed during appendectomies,¹ there was renewed interest in these formations in the 1960s when it was hypothesised that these bodies were specific for sarcoidosis.^{4,7}

Subsequent research has demonstrated Hamazaki-Wesenberg bodies to be no more prevalent in sarcoidosis than in other conditions; likewise, theories proposing a mycobacterial aetiology have been similarly

discounted.³ Whereas the precise origins of these phenomena remain elusive, mistaking these structures for pigmented fungal organisms, particularly in cases where patients are immunocompromised and the threshold for infectious diagnoses is very low,² is a diagnostic pitfall with severe consequences. Recognising Hamazaki-Wesenberg bodies can be complicated by the variable size and close proximity of such bodies to one another, which can mimic budding yeast,⁸ and positive staining with both Gomori methenamine silver (GMS) and predigested periodic acid-Schiff (PASD), both of which are commonly used for fungi.²

Accurate diagnosis of Hamazaki-Wesenberg bodies thus relies on the diagnosing pathologist meticulously examining the morphology of any potential fungal organisms located on H&E stained slides, and maintaining this diagnostic vigilance when examining any additional stains ordered. While these bodies typically show a yellow-brown colouring on H&E, this can vary substantially; therefore, supplementary stains may be of assistance (fig 1). Since both Hamazaki-Wesenberg bodies and numerous fungal organisms react with GMS and predigested PAS, stains such as the Fontana-Masson silver or acid-fast staining for ceroid may be helpful in differentiating a fungus from a viceroy.² The ceroid nature of Hamazaki-Wesenberg bodies has been postulated by Sieracki and Fisher, and acid-fast staining for ceroid (long Ziehl-Neelson acid fast) has been shown to react with the bodies, whereas standard Ziehl-Neelson acid-fast technique may be weakly positive or negative.^{2,3,9}

The Fontana-Masson silver stain may be particularly useful in such diagnostic dilemmas given that, with the exception of *Cryptococci*, fungi are generally non-reactive to this stain whereas Hamazaki-Wesenberg bodies do react.²

Take-home message

Hamazaki-Wesenberg bodies can be found in lymph nodes in many diverse disease processes and supplementary stains can help differentiate them from fungi, sparing patients unnecessary exposure to antifungal medications.

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For this retrospective case report patient identifying information was used solely to confirm that patients' medical history was negative for sarcoid disease. The diagnosis and treatment of the patients was unchanged by this report, and no records were kept linking patient identifying information to material discussed in this report.

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SHORT REPORTS

Gastric MALT lymphoma with t(14;18)(q32;q21) involving IGH and BCL2 genes that responded to *Helicobacter pylori* eradication

Four recurrent chromosomal translocations are recognised in mucosa-associated lymphoid tissue (MALT) lymphomas: t(11;18)/API2-MALT1, t(1;14)/IGH-BCL10, t(14;18)/IGH-MALT1 and t(3;14)/IGH-FOXP1. In contrast, t(14;18)/IGH-BCL2, the genetic hallmark of follicular lymphoma, has been observed in only rare cases of MALT lymphoma. Oesophagogastrroduodenoscopy revealed an ulcer in erythematous granular mucosa at the gastric corpus in a 55-year-old man. A diagnosis of MALT lymphoma was made on the basis of typical histological and immunohistochemical features of biopsy specimens: a diffuse infiltrate of centrocyte-like cells surrounding reactive lymphoid follicles and forming lymphoepithelial lesions, and a CD20+, IgD–, CD5–, CD10–, Bcl6–, cyclinD1– immunophenotype. Four months after the successful eradication of *Helicobacter pylori*, there was endoscopic regression with probable minimal residual disease detected by biopsy, but histological relapse was recognised 12 months after eradication. Interphase fluorescence *in situ* hybridisation revealed t(14;18)/IGH-BCL2, but not the translocations typically seen in MALT lymphoma. This is the first report of a gastric MALT lymphoma with t(14;18)/IGH-BCL2 that responded to *H. pylori* eradication.

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT

lymphoma) is genetically characterised by the recurrent translocations t(11;18)(q21;q21)/API2-MALT1, t(1;14)(p22;q32)/BCL10-IGH, t(14;18)(q32;q21)/IGH-MALT1 and t(3;14)(p14;q32)/FOXP1-IGH.^{1–2} Recent evidence suggests that at least some of these translocations may be associated with distinct clinicopathological features.^{1–3} The t(14;18)(q32;q21)/IGH-BCL2 is found in the majority of follicular lymphomas and some diffuse large B-cell lymphomas.⁴ However, MALT lymphomas carrying this translocation are extremely rare and their clinical features are virtually unknown.

Case report

A 55-year-old asymptomatic man underwent oesophagogastrroduodenoscopy (OGD) as screening for gastric carcinoma. OGD revealed an open ulcer with surrounding granular erythematous mucosa in the upper corpus (fig 1A). Histological examination of biopsy specimens taken adjacent to the ulcer margin and from nearby erythematous spots showed a diffuse infiltrate of centrocyte-like and small lymphocyte-like cells surrounding reactive lymphoid follicles in a marginal zone distribution, forming prominent lymphoepithelial lesions (fig 2A). Monocytoid differentiation and plasmacytoid cells with Dutcher bodies were also observed. Immunohistochemistry showed the neoplastic cells to express CD20, CD79a and Bcl2, but not CD3, CD5, CD10, CD43, Bcl6, cyclinD1 or IgD (fig 2A). On the basis of these findings, a diagnosis of MALT lymphoma was made.

Staging investigations including endosonography,⁵ CT of the chest and abdomen, colonoscopy, small bowel follow-through, peripheral blood and bone marrow examination, and ¹⁸F-fluorodeoxyglucose positron emission tomography showed Lugano stage I disease.⁶ *H. pylori* was detected by the rapid urease test, histology and serology, and was eradicated with rabeprazole 40 mg/day plus amoxicillin 2000 mg/day for 2 weeks. Successful eradication of *H. pylori* was confirmed by [¹³C]urea breath test 2 months after treatment. Serological investigation for hepatitis C virus (HCV) infection was negative.

Follow-up OGD 4 months after eradication showed disappearance of the initial lesion with small residual scars (fig 1B). Several biopsy specimens obtained from the scars and the surrounding mucosa displayed mildly oedematous lamina propria with scattered plasma cells and eosinophils, but no evidence of lymphoma.

Figure 1 (A) Pretreatment oesophagogastrroduodenoscopy (OGD) revealed a superficial lesion comprising an open ulcer, multiple scars and erythematous granular mucosa on the posterior wall of the upper corpus. (B) Follow-up OGD 4 months after *Helicobacter pylori* eradication showed regression of the initial lesion with multiple scars and mildly erythematous mucosa. The arrow indicates a healed scar from the ulcer in (A). Informed consent was obtained for publication of this figure.

However, one specimen, taken from an erythematous spot, contained aggregates of small lymphoid cells (fig 2B), consistent with histologically defined probable minimal residual disease (pMRD).⁷ Further OGD and biopsy at 7 months also showed endoscopic regression with pMRD. However, histological relapse, defined as a definite lymphomatous infiltrate, was recognised at 12 months, despite the absence of endoscopically evident lymphoma. At this time, [¹³C]urea breath test, rapid urease test and histology all remained negative for *H. pylori*. Follow-up investigations at 15, 18, 21 and 24 months showed only atrophic changes endoscopically, although focal histological evidence of lymphoma was seen on several of the biopsy specimens taken. The patient is currently under careful observation without any additional treatment.

Molecular genetic findings

The presence of MALT lymphoma-associated chromosome translocations was assessed by interphase fluorescence *in situ* hybridisation (FISH) on formalin-fixed, paraffin-embedded tissues.² FISH probes were obtained from Vysis/Abbott, Maidenhead UK, except for the FOXP1 and BCL10 break-apart probes (kindly provided by Dr A Banham, Oxford, and Professor R Siebert, Kiel, respectively). FISH on pretreatment specimens showed a split signal with IGH and BCL2 break-apart probes but not with MALT1, BCL10, BCL6, CCND1 or FOXP1 probes. FISH using a dual-colour dual-fusion translocation probe showed co-localisation of IGH and BCL2 signals (fig 2C) indicating the presence of t(14;18)/IGH-BCL2. t(14;18)/IGH-BCL2 was also identified in follow-up biopsy specimens, including those showing pMRD. Extra copies were observed by FISH with the MALT1 break-apart probe and with the centromere-specific probe for chromosome 18, but not with BCL2 or IGH probes. These findings suggest the presence of partial trisomy 18.

Discussion

Although the case reported in this study is positive for t(14;18)/IGH-BCL2, the diagnosis of MALT lymphoma is beyond doubt. This is supported by the characteristic histological and immunohistochemical findings: centrocyte-like cells surrounding reactive lymphoid follicles, prominent lymphoepithelial lesions, and the CD20+, CD5–, CD10–, Bcl6–, IgD– and