INTRODUCTION

Autoimmune pancreatitis (AIP) is a fibroinflammatory condition characterized by tumefactive lesions, a dense lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells, storiform fibrosis and often but not always, elevated serum IgG4 concentrations [1]. Although Yoshida et al discovered similar pathology affecting the pancreas in Japan in 1995 and coined the term autoimmune pancreatitis (AIP) [2], the clinical characteristics of this condition were described as early as 1961 [3]. The disease was not recognized as a systemic disease until 2003, when extrapancreatic manifestations were identified in patients with AIP [4]. This has resulted in a change in nomenclature to IgG4 associated systemic disease (ISD), which encompasses all diseases associated with a positive IgG4 serology or histology. There has been increasing evidence that AIP/ISD exists in non-Japanese populations [5]. To aid diagnosis of this condition, various criteria have been derived by different groups. More recently, AIP caused by neutrophilic granulocyte infiltration and not related to IgG4 has been reported in the Western World [6]. Chari et al referred to IgG4 related AIP as type I (with lymphoplasmacytic infiltrate) and granulocyte lesions (non IgG4 related) of AIP as type II (idiopathic duct centric type with granulocyte epithelial cells) [7]. We report our experience in the diagnosis and management of this condition in the North East of England including long term follow up.
METHODS

Freeman hospital is a tertiary care hospital in North East England and is the regional referral centre for benign and malignant pancreatobiliary diseases. All patients seen in our hospital and diagnosed with AIP from January 2005 to August 2013 were included in the study. There are at least three well-known sets of criteria, i.e. Japanese [8], Korean [9] and Mayo Clinic criteria [10] for diagnosing ISD/AIP. For the purposes of this study, we have applied the Mayo clinic revised HISORt criteria (“HISORt” for histology, imaging, serology, other organ involvement and response to corticosteroid therapy) and the International Consensus Diagnostic Criteria (ICDC) for diagnosis of our patients [10]. Type I and Type II were also defined by the criteria set by Sugumar et al [7].

Data were obtained from a prospectively maintained database of all patients referred to our unit with suspected AIP. Data collected included the age, sex, date of diagnosis, IgG4 levels at time of diagnosis and follow up, CA19-9 levels before and after treatment and longterm follow up data. All patients underwent contrast enhanced computed tomogram (CT) scan as the baseline investigation (Fig. 1). Some patients who were referred to our hospital from regional hospitals had also undergone magnetic resonance cholangiopancreatogram (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP). MRCP was mainly used to document biliary and pancreatic strictures (Fig. 2). When clinically indicated, patients also underwent endoscopic ultrasound (EUS) examination to image the pancreas and EUS-guided fine needle aspiration (FNA) if necessary. Patients were managed according to standard clinical practice till the diagnosis of ISD was investigated and confirmed. All patients were discussed in a dedicated hepatobiliary and pancreatic multidisciplinary meeting to ensure the correct diagnosis. Following confirmation of diagnosis as per the HISORt criteria, the patients were commenced on prednisolone 40mg per day in selected patients. The dosage of the steroids was gradually tapered over 4–6 weeks. Treatment response was assessed by improvement in patient’s symptoms, liver function tests (LFT), serological and radiological parameters. Azathioprine was the first line for treatment failures or relapses following steroid withdrawal. If the patients were steroid resistant or azathioprine intolerant, other forms of immunosuppression was considered. Radiological investigations were repeated after 8–10 weeks or sooner to ensure improvement of findings. All patients have been followed up to date.

RESULTS

Autoimmune pancreatitis was diagnosed in 22 patients during the study period. All our patients met at least 3 of the 5 HISORt diagnostic criteria. Six patients met 3 criteria, 10 patients met 4 criteria and one patient all 5 criteria (Table 1).

If the ICDC was applied, 20 patients had definite Type 1 AIP, 1 patient had probable Type 1 AIP and 1 patient had definite Type II AIP. There were 21 male and 1 female patients. The mean age of the group was 64.8 years (range: 43–84). All patients, except one (an Asian Indian) were Caucasians. The main presenting symptoms were abnormal LFTs without jaundice (17 patients), weight loss (9), acute abdominal pain without hyperamylasemia (6), vomiting (3), lethargy (1), itching (1) and altered bowel habits (1 patient). The initial diagnoses considered at presentation were autoimmune pancreatitis (10), pancreatic cancer (6), cholangiocarcinoma (3), chronic pancreatitis (1), primary sclerosing cholangitis (1) and retroperitoneal sarcoma (1). Mean alkaline phosphatase (ALP) level was 456 U/L (range 52–1270, NV 40–120 U/L) and mean alanine transaminase (ALT) was 129.7 U/L (range 15–386, NV 21–40 U/L). Mean bilirubin was 97 micromoles/L (range 5–354, NV 5-17 micromoles/L). CA 19-9 was elevated in 16 patients (mean 262 kU/L; range 1–2127 kU/L; NV 0–33 kU/L) at presentation.

Total IgG was elevated in 10 patients (mean 19.96 g/L; range 15.8–42, NV 5.8–5.4 g/L) and 14 (64%) had an elevated IgG4 level (mean 10.5 g/L; range 3.4–31 g/L , NV 0–2.4 g/L). One patient with Sjögren’s syndrome had anti-centromere antibodies and another patient was anti-Ro and anti-La positive. Four patients underwent surgery. Two of them had surgery for chronic pancreatitis and a mass in the pancreatic head, suspicious of pancreatic cancer; one had emergency gastro-enterostomy for duodenal obstruction and one had a hepatico-jejunostomy and pancreatic biopsies as part of a palliative procedure for suspected locally advanced inoperable pancreatic malignancy. Three patients underwent laparoscopic pancreatic biopsy for diagnostic confirmation. Histological examination of the resected/biopsy specimen was pathognomonic for AIP in all these cases (Fig. 3a).

Extrapancreatic involvement consisted of bile duct strictures (14 patients), gall bladder and peripancreatic infiltration (2), duodenal infiltration and obstruction (1), stomach wall (1) pericardial involvement (1); renal/pleural involvement (1) and retroperitoneal fibrosis (2 patients). Association with other autoimmune diseases was also noted: Sjögren’s syndrome (1 patient) and Raynaud’s disease (1 patient).

The radiological findings of CT and MRCP are summarized in Table 1. CT findings documented an enlarged head of pancreas (11 patients) (Fig. 1), enlarged body/tail/uncinate process of pancreas (7 patients), thickening/stricturing of extrahepatic bile ducts with dilatation and increased uptake of contrast (11 patients), intrahepatic bile duct structural/ dilatation and thickening (10 patients), focal pancreatitis (1), gall bladder mass (2), mass in the mesentery (1) and pancreatic calcification (2 patients). Eight patients also had MRCP for investigation for obstructive jaundice. All of them had diffuse intra and extrahepatic stricturing of the bile ducts with increased uptake of gadolinium contrast by the duct walls. Five patients had ERCP performed elsewhere prior to referral for management of obstructive jaundice. All 5 of them had extrapancreatic biliary strictures (Fig. 2a) and 4 had plastic stent insertions at the procedure. Biliary brushings were not specifically stained for IgG4 cells and were inconclusive with no evidence of malignancy. Endoscopic ultrasound (EUS) was performed in 12 patients. Seven patients had a diffusely enlarged head of the pancreas (HoP), 1 had a retroperitoneal mass, 4 had some EUS features of chronic pancreatitis (calcification, hyperechoic stranding, hypoechoic areas), 1 had a mass in HoP, 1 had atrophic pancreas. Seven patients were documented to have a diffuse thickening of the common
<table>
<thead>
<tr>
<th>No.</th>
<th>Age (years)</th>
<th>CA19.9 (Normal = 0–33 KU/L)</th>
<th>IgG4 (Normal = 0–2.4g/L)</th>
<th>CT/MRCP</th>
<th>Histology</th>
<th>Other organ involvement - OOI</th>
<th>Response to steroids - Rt</th>
<th>HISORt criteria</th>
<th>ICDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>77</td>
<td>1109</td>
<td>13.34</td>
<td>Enlarged HoP with intra and extrahepatic bile duct strictures</td>
<td>N/A</td>
<td>Bile duct</td>
<td>Yes</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>2127</td>
<td>28.6</td>
<td>Mass in HoP involving duodenum/gall bladder</td>
<td>Fibrous plasma cells with IgG4</td>
<td>Bile duct, pericardium, gall bladder</td>
<td>Yes</td>
<td>5/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>3</td>
<td>77</td>
<td>124</td>
<td>11.6</td>
<td>Enlarged HoP with distal bile duct structure</td>
<td>N/A</td>
<td>Bile duct</td>
<td>Yes</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>4</td>
<td>83</td>
<td>1</td>
<td>3.4</td>
<td>Intrahepatic strictures pancreatic calcification</td>
<td>N/A</td>
<td>Bile duct</td>
<td>Yes</td>
<td>3/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>5</td>
<td>82</td>
<td>117</td>
<td>5.22</td>
<td>Enlarged HoP with intrahepatic strictures</td>
<td>N/A</td>
<td>Bile ducts</td>
<td>Yes</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>6</td>
<td>79</td>
<td>12</td>
<td>1.87</td>
<td>Intrahepatic strictures with gall bladder mass</td>
<td>Plasma infiltrate with IgG4 + Gall bladder, bile duct</td>
<td>Gall bladder, bile duct</td>
<td>Yes</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>7</td>
<td>57</td>
<td>11</td>
<td>5.67</td>
<td>Enlarged HoP intrahepatic strictures</td>
<td>N/A</td>
<td>None</td>
<td>Yes</td>
<td>3/5</td>
<td>Probable AIP 1</td>
</tr>
<tr>
<td>8</td>
<td>68</td>
<td>64</td>
<td>6.77</td>
<td>Enlarged HoP in intrahepatic strictures</td>
<td>N/A</td>
<td>Bile duct</td>
<td>Yes</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>9</td>
<td>66</td>
<td>105</td>
<td>2.01</td>
<td>Enlarged HoP + distal bile duct structure</td>
<td>Fibrosis, IgG4 + plasma cells</td>
<td>None</td>
<td>N/A</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>10</td>
<td>46</td>
<td>33</td>
<td>0.73</td>
<td>Enlarged HoP, bile duct stricture</td>
<td>Fibrosis, IgG4 + plasma cells</td>
<td>Bile duct</td>
<td>Yes</td>
<td>3/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>11</td>
<td>64</td>
<td>63</td>
<td>2.76</td>
<td>Mass HoP, intrahepatic bile duct strictures</td>
<td>N/A</td>
<td>Bile ducts</td>
<td>Yes</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>12</td>
<td>61</td>
<td>4</td>
<td>1.89</td>
<td>Mass in HoP</td>
<td>Fibrosis, IgG4 + plasma cells</td>
<td>None</td>
<td>Yes</td>
<td>3/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>13</td>
<td>50</td>
<td>13</td>
<td>4.23</td>
<td>Enlarged HoP, bile duct stricture</td>
<td>N/A</td>
<td>Bile duct, Sjogren’s syndrome</td>
<td>Yes</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>14</td>
<td>43</td>
<td>2</td>
<td>0.27</td>
<td>Mass in HoP</td>
<td>Granulat epithelial cells – Idiopathic duct centric type</td>
<td>None</td>
<td>N/A</td>
<td>3/5</td>
<td>Definite AIP II</td>
</tr>
<tr>
<td>15</td>
<td>61</td>
<td>91</td>
<td>24.6</td>
<td>Intra hepatic bile duct strictures</td>
<td>N/A</td>
<td>Bile duct</td>
<td>Yes</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>16</td>
<td>67</td>
<td>48</td>
<td>1.67</td>
<td>Enlarged HoP, Bile duct stricture</td>
<td>N/A</td>
<td>Bile duct</td>
<td>Yes</td>
<td>3/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>17</td>
<td>83</td>
<td>296</td>
<td>31</td>
<td>Enlarged HoP</td>
<td>N/A</td>
<td>None</td>
<td>Yes</td>
<td>3/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>18</td>
<td>58</td>
<td>132</td>
<td>9.8</td>
<td>Enlarged HoP</td>
<td>N/A</td>
<td>None</td>
<td>Yes</td>
<td>3/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>19</td>
<td>58</td>
<td>88</td>
<td>3.96</td>
<td>Enlarged HoP, intrahepatic strictures</td>
<td>N/A</td>
<td>Bile duct</td>
<td>Yes</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>20</td>
<td>65</td>
<td>46</td>
<td>1.2</td>
<td>Enlarged HoP</td>
<td>N/A</td>
<td>None</td>
<td>Yes</td>
<td>3/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>21</td>
<td>68</td>
<td>141</td>
<td>9.4</td>
<td>Enlarged HoP, intrahepatic strictures</td>
<td>N/A</td>
<td>Bile duct</td>
<td>Yes</td>
<td>4/5</td>
<td>Definite AIP 1</td>
</tr>
<tr>
<td>22</td>
<td>58</td>
<td>42</td>
<td>6.8</td>
<td>Enlarged HoP, intrahepatic strictures</td>
<td>Fibrosis, IgG4 + plasma cells</td>
<td>Bile duct, kidney, pleura</td>
<td>Yes</td>
<td>5/5</td>
<td>Definite AIP 1</td>
</tr>
</tbody>
</table>

IgG- Immunoglobulin; CT – Computed Tomography; MRCP – Magnetic Resonance Cholangiopancreatogram; ICDC – International Consensus Diagnostic Criteria; HoP – Head of pancreas ; N/A – Not applicable; AIP – Autoimmune pancreatitis

bile duct associated with hyperechoic duct walls. None of the patients was found to have evidence of peri-pancreatic or hilar lymphadenopathy. Vascular invasion (encasement of the superior mesenteric artery) was seen in two patients on EUS. EUS guided fine needle aspiration (FNA) was performed in four patients. Cytological examination confirmed lympho-
plasmacytic infiltrate in 1 patient, indeterminate (1 patient; mass encasing superior mesenteric artery, underwent laparoscopic biopsy later which confirmed diagnosis), suspicious for malignancy (1 patient; enlarged HoP with CBD stricturing; histological confirmation after Whipple resection), insufficient (1 patient; ERCP at the referring hospital with brushings suggestive of malignancy; underwent laparoscopic biopsy which confirmed diagnosis – Fig. 3 a, b). The final diagnosis was Type I AIP (21 patients), Type II AIP (1 patient); 5/22 (23%) were diagnosed as being diabetic on presentation and 9/22 (41%) had exocrine insufficiency based on low fecal elastase levels.

Eighteen patients (82%) were initiated on steroids. Eleven patients had an elevated bilirubin (mean 123 mmols/L; range 42–289). Elevated total IgG was found in 10 patients (26.2 g/L, range: 15.8 – 42) and elevated IgG4 (10.69; range 2.76–31) in 10/13 patients in the subgroup receiving steroids. The remaining four patients did not require any steroid therapy as they had self-limiting disease.

Follow up data

All patients have been followed up to date. The mean follow up period was 36.94 months (7–94 months). All 18 patients experienced alleviation of symptoms (abdominal pain or discomfort, fatigue) within 2 weeks of steroid initiation. Twelve patients with abnormal LFTs had normal LFTs by the fourth week. Four patients had sub-optimal response. The first patient did not show complete resolution of LFTs with steroids and Azathioprine was initiated with a resolution of LFTs subsequently on follow-up (Fig. 2b). The second patient was only partially steroid responsive from the outset and was treated with Azathioprine, 6-Mercaptopurine and Mycophenolate Mofetil. This patient developed chronic liver disease and portal hypertension due to secondary biliary cirrhosis. He was taken off immunosuppression due to chronic encephalopathy and was on low dose steroids. He unfortunately died due to end stage liver failure. Five patients (25%) relapsed after steroid withdrawal and all of them were successfully managed with the initiation of Azathioprine. No pancreaticobiliary malignancies were diagnosed in the follow up period. The patients who had elevated CA 19-9 levels have normal values after treatment and none of them developed malignancy during the follow up period.

**DISCUSSION**

Autoimmune pancreatitis is a condition which was first reported in Japan and its existence in the western world was debated until recently [4, 11]. This paper adds to the available data from the United States [5, 10, 12, 13] and Europe [14-16] and supports the fact that this condition is not confined to certain geographical regions in the world. There has been a case series from the UK in the literature [17] and patients from the UK have been reported as part of large multicentre series [18].

Though our first case was diagnosed in 2005, there has been increased awareness of this condition, which has resulted in a gradual increase in the diagnosis. The mean age of presentation (64 years) and male preponderance is similar to the published literature [10, 19]. The commonest clinical presentation of patients with AIP is either jaundice or abnormal LFTs associated with weight loss. In our series, 77 % (17 patients) presented with jaundice and 73 % (16 patients) had cholestasis (LFTs) at presentation.

Elevated IgG4 levels at presentation were documented in 64% in our series, similar to the previous series from UK (17). Another large series from Korea reported elevated IgG4 levels in 47% of their patients with AIP [20]. The sensitivity of elevated
IgG4 levels in diagnosing ISD is reported to be between 64% and 95% [17, 21, 22]. Although the Japanese studies report that IgG4 elevation is highly specific and sensitive for AIP [22], raised serum IgG4 is also seen in pancreatic cancer and other forms of chronic pancreatitis [12]. Elevation of IgG4 levels (≤2 fold) can be seen in up to 10% of subjects without AIP including pancreatic cancer [23].

In another study, serum IgG4 levels were also found to be elevated in cholangiocarcinoma and some had a more than 2-fold rise [24]. These studies reiterate the fact that serum IgG4 levels should never be used in isolation for diagnosis of AIP.

CA 19-9 levels may also be elevated in AIP [20, 25, 26]. In our series, CA 19-9 levels were elevated in 16 (73%) of the patients. Another similar study examining the behavior of CA 19-9 in patients suffering from AIP found elevated levels in 47% of their patients prior to treatment [27]. These studies propose that elevated CA19-9 is a result of cholestasis, cholangitis or pancreatitis which returns to normal after steroid treatment [20, 28] but it is vital to ensure that malignancy has been ruled out as it remains the most common cause for an elevated CA19-9.

Autoimmune pancreatitis is most commonly misdiagnosed as pancreatic cancer and it is imperative to differentiate these conditions to prevent unnecessary surgery [29]. Cancer was suspected initially in patients with AIP in up to 73% of the cases in one study [9]. Indeed, in another Japanese study, 20% of the cases with AIP were misdiagnosed as having pancreatic malignancies [28]. Conversely, experience from the Mayo clinic suggested that up to 15% of patients with pancreatic cancer were misdiagnosed as having AIP on CT imaging alone [29]. In our series, malignancy was suspected in 41% of the patients (pancreatic cancer suspected in 6 and cholangiocarcinoma in 3 patients). In a large Korean series of 67 patients, surgery was carried out for suspected pancreatic cancer in 18% of patients [30]. Four patients (18%) underwent surgery in our series for suspected cancer and two of them had bypass procedures performed (hepatico-jejunostomy and gastroenterostomy) as a part of the palliative operation for suspected locally advanced inoperable pancreatic malignancy. We now have a better understanding and a high level of suspicion in these cases thus avoiding unnecessary surgery in a later period.

Misdiagnosing AIP in patients with cancer is a major worry, as delay in diagnosis is likely to close the already narrow window of curative surgical options in these patients [31]. We discuss all our cases in a multi-disciplinary setting to ensure correct diagnosis. The Mayo HISORT, Japanese, Korean or more recently the ICDC [32] criteria should be followed strictly in patients as these help to differentiate malignancy from AIP.

Imaging findings in AIP include presence of focal or diffuse pancreatic gland enlargement, atrophy and calcification [33, 34]. The biliary tract is the commonest extrapancreatic site to be involved (in 30–90% of the cases) and although both the intra and extrahepatic bile ducts can be too, the distal common bile duct is the most common site of involvement [33, 34]. Pancreatic gland abnormality on imaging was seen in 90% of patients and biliary involvement was noted in 68% in our series. Another Japanese series noted biliary involvement in 58% of patients [35]. Intrahepatic bile duct stricturing is now being increasingly recognized as a part of AIP [34]. In our series, 41% of patients (9 patients) were demonstrated to have diffuse intrahepatic strictures at presentation. Patients with AIP have been noted to have long strictures with prestenotic dilatation in contrast to primary sclerosing cholangitis where beading and peripheral duct pruning were more common.

Cross sectional imaging, i.e. CT and MR remains the ideal modality to diagnose AIP. However, EUS can also contribute to the diagnosis in selected cases [36]. Endoscopic ultrasound (EUS) features of AIP consist of either diffuse increase in the size of the pancreas (diffuse form of AIP) or focal enlargement of a part of the pancreas (focal form of AIP). This may be associated with echogenic interlobular septae, thickened gland border, narrowing/stricturing of the pancreatic duct and a generally poor echo texture of the pancreas. The bile ducts may demonstrate uniform wall thickening (“sandwich pattern” – echo poor intermediate layer with hyperechoic outer and inner layers) and the gall bladder may also be dilated with thickened walls. There may be enlarged lymph nodes seen along with loss of interface between the pancreas and portal vessels. Buscarini et al [36] also noted that the thickening of the bile ducts and pancreatic ducts and loss of interface of the pancreas with the portal veins were best seen on EUS compared to other radiological modalities. In our series, 55% (12 patients) who underwent EUS demonstrated typical EUS features of duct wall thickening. A suspicion of the diagnosis of AIP was raised at EUS independently in 67% (8 out of 12 patients). Often, the diagnosis of AIP can be difficult using EUS–FNA cytology alone (as in our series) and this may require a larger specimen.
which can be obtained with EUS-guided biopsy [37]. With newer needles for tissue acquisition, the histopathologists can also stain for IgG4 thereby avoiding unnecessary minor surgery for diagnosis. Newer techniques of molecular analysis utilizing microsatellite loss and K-ras mutation performed on the FNA cytology specimens may help in differentiating benign from malignant pancreatic masses in the future [38, 39].

The diagnosis of Type II AIP is controversial and a well documented case has not previously been reported in the UK. The condition was only first described in 2003 [40]. Autoimmune pancreatitis with neutrophil infiltration in the epithelium of the pancreatic duct (idiopathic duct centric chronic pancreatitis: IDCP, or granulocyte epithelial lesions: GELs) has been reported by American (7) and Italian [41] pathologists. We diagnosed on histopathology one young male patient (43 years) who presented with a mass in the head of the pancreas, and an inconclusive EUS-FNA and subsequently underwent a Whipple's operation, to have IDCP/GEL type of involvement of the pancreas confirming the presence of this condition in the UK.

Autoimmune pancreatitis characteristically responds to steroid therapy. Spontaneous resolution without treatment has also been noted [10]. It is the intense inflammatory component of the disease that responds to steroid therapy; the fibrosis often permanently disfigures, damages and sometimes destroys the organ [42]. While structural normalcy appears to be restored sometimes following steroid therapy, it often results in glandular atrophy with or without pancreatic insufficiency [43, 44]. Although diabetes and steatorrhoea can develop after AIP, it is unclear if treatment with steroids reduces long-term incidence of pancreatic exocrine and endocrine insufficiency [14].

Relapse rates (27% in our study) were also no different to a long-term follow up data from a large cohort of Japanese patients. Relapse is common (40-53% of patients) and is predicted by the presence of proximal extra- and intrahepatic biliary stricturing and HLA DQβ1 [18]. There is limited data on the role of immunosuppression in patients with AIP as radiological and clinical improvement may also occur without any treatment and there is no placebo controlled trial available to confirm the benefit of steroids [44]. However, the recently published Mayo treatment algorithm for relapsing AIP may help us guide for treatment but needs to be validated [45].

The data on mortality directly linked to autoimmune pancreatitis is unclear and one of our patients died due to intractable disease. AIP is a chronic inflammatory disease and, similar to other conditions, a group of these patients should be prone to develop malignancy in the longer term. However, there is very limited data on the incidence of malignancy in AIP. Shiokawa et al [46] reported that patients with AIP are at high risk of having various cancers. The highest risk for cancer in the first year after AIP diagnosis and absence of AIP relapse after successful treatment of the coexisting cancers suggest that AIP may develop as a paraneoplastic syndrome in some patients. More data is required to corroborate this finding.

CONCLUSIONS

Autoimmune pancreatitis is being increasingly recognized in the British population. Extrapancreatic involvement, particularly extrahepatic biliary involvement is a frequent feature. Intrahepatic stricturing is more common than was previously recognized. It is imperative to first exclude malignancy which is the much commoner diagnosis. Early recognition of this condition can prevent unnecessary interventions. Steroid responsiveness is characteristic but should never be used as a substitute to an aggressive search for malignancy. Serum IgG4 levels are also elevated in patients with pancreatic cancer and chronic pancreatitis. Before initiating steroids a marker should be identified that can be followed up to assess objective response during treatment. Diagnosis should always be based on accepted criteria as this significantly reduces the chances of missing malignancy. Awareness of this relatively rare condition and a multi-disciplinary team approach will help us to diagnose and treat this condition more effectively thereby reducing unnecessary interventions.

Conflicts of interest. No conflict to declare.

Authors’ contribution. SC, MN and KO conceptualized the study and were involved in the clinical care of the patients. SC prepared the proforma, collected and analyzed the data. JS reviewed the radiology and BH reviewed the histopathology. All authors contributed to the drafting of the paper and revising it for intellectual content.

REFERENCES

11. Research Committee to establish diagnostic criteria and development of treatment for systemic IgG4-related sclerosing disease; Research


