None declared, Selim Aractangi: None declared, Beatrice Banville Speakers bureau: Lilly, Novartis, Laurent Beaugerie: None declared, Francis Berenbaum Grant/research support from: TRB Chemedica (through institution), MSD (through institution), Pfizer (through institution), Consultant of: Novartis, MSD, Pfizer, Lilly, UCB, Abbvie, Roche, Servier, Sanofi-Aventis, Flexion Therapeutics, Expanscience, GSK, Biogen, Nordic, Sandoz, Regeneron, Gilead, Bone Therapeutics, Regulaxis, Peptinov, 4P Pharma, Paid instructor for: Sandoz, Speakers bureau: Novartis, MSD, Pfizer, Lilly, UCB, Abbvie, Roche, Servier, Sanofi-Aventis, Flexion Therapeutics, Expanscience, GSK, Biogen, Nordic, Sanofi, Pfizer, Gilead, Sandoz, Julien Champey; None declared, Olivier Chazourilles: None declared, Christophe Corpechot: None declared, Bruno Fautrel Grant/research support from: Abbvie, Lilly, MSD, Pfizer, Consultant of: Abbvie, Biogen, BMS, Boehringer Ingelheim, Celgene, Lilly, Janssen, Medac, MSD France, Nordic Pharma, Novartis, Pfizer, Roche, Sanofi Aventis, SOBI and UCB, Arsenе Mekinian: None declared, Elodie Regnier: None declared, David Sandroni: None declared, Joe-Elie Salem: None declared, Jérémie Sel-LAM: None declared, Philippe Seksik: None declared, David Klatzmann Consultant of: LTOO Pharma

Background: In the acute phase of adult-onset Still's disease (AOSD), elevated levels of proinflammatory cytokines (IFN-γ) are shown. Moreover, IFN-γ impacts on activating macrophages which play a crucial role in the pathogenesis of AOSD. Natural killer (NK) cells and T helper cells are in charge of secreting IFN-γ in the innate and adaptive immune systems of disease, respectively. However, the features of their IFN-γ-producing variation depending on disease activity are still uncertain in AOSD;

Objectives: We investigated characteristics of IFN-γ-producing CD4+ T cells and NK cells in patients with AOSD.

Methods: Twenty-four patients in the acute phase of AOSD (active AOSD), 8 of them after treatment (remission), and 12 healthy controls (HC) were recruited in this study. Peripheral blood mononuclear cells and serum samples were provided from them for the experimental analysis. Flow cytometry was used for analyzing CD4+ T cells, CD4+ regulatory T cells (Tregs), NK cells, and their intracellular IFN-γ expression as well as suppression assay of Tregs. The serum concentration of interleukin-18 (IL-18) was measured using commercially available ELISA kit. Relationship between the analyzed data and clinical findings related to disease activity were statistically evaluated.

Results: IFN-γ expression in CD4+ T cells was significantly higher in active AOSD than in HC (p < 0.05). Tregs also significantly indicated higher expression of IFN-γ in active AOSD than in HC (p < 0.0001), and moreover, Tregs were significantly impaired in their suppression ability (p < 0.05). In both CD4+ T cells and Tregs, expression of IFN-γ was significantly correlated with serum ferritin levels in active AOSD (p < 0.05). IFN-γ expression in CD4+ T cells was significantly higher in patients with splenomegaly than those without that (p < 0.05). The proportion of NK cells was significantly lower in active AOSD than in HC (p < 0.0005), whereas IFN-γ expression in NK cells was significantly higher in active AOSD than in HC (p < 0.0005). The number of NK cells and IFN-γ expression in NK cells had inverse relationship with serum ferritin levels in active AOSD (p < 0.05 and p < 0.005, respectively). Increased number of NK cells and their decreased expression of IFN-γ were significantly demonstrated in remission (p < 0.05). In the analyses of NK cell subsets, lower expression of IFN-γ in CD56dim NK cells than in CD56bright NK cells were also observed (p < 0.05). In remission, IFN-γ expression was significantly decreased in CD56dim NK cells (p < 0.05) despite no significant recovery of that in CD56bright NK cells (p = 0.311). Meanwhile, increased expression of IFN-γ in CD56dim NK cells was demonstrated in only patients who were treated with biologics. Although serum levels of IL-18 were significantly higher in active AOSD than in remission and HC; however, they had no significant correlations with any analyzed data.

Conclusion: CD4+ T cells and NK cells promote IFN-γ expression in the acute phase of AOSD. Meanwhile, increased expression of IFN-γ in CD4+ T cells and decreased number of NK cells were correlated with serum ferritin levels, suggesting that they are indicators of disease activity. Furthermore, high disease activity may impact on the alteration of IFN-γ-producing balance in two distinct population of NK cells, and the plasticity of Tregs leading to defect in suppression ability.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5733

None declared, Selim Aractangi: None declared, Beatrice Banville Speakers bureau: Lilly, Novartis, Laurent Beaugerie: None declared, Francis Berenbaum Grant/research support from: TRB Chemedica (through institution), MSD (through institution), Pfizer (through institution), Consultant of: Novartis, MSD, Pfizer, Lilly, UCB, Abbvie, Roche, Servier, Sanofi-Aventis, Flexion Therapeutics, Expanscience, GSK, Biogen, Nordic, Sandoz, Regeneron, Gilead, Bone Therapeutics, Regulaxis, Peptinov, 4P Pharma, Paid instructor for: Sandoz, Speakers bureau: Novartis, MSD, Pfizer, Lilly, UCB, Abbvie, Roche, Servier, Sanofi-Aventis, Flexion Therapeutics, Expanscience, GSK, Biogen, Nordic, Sanofi, Pfizer, Gilead, Sandoz, Julien Champey; None declared, Olivier Chazourilles: None declared, Christophe Corpechot: None declared, Bruno Fautrel Grant/research support from: Abbvie, Lilly, MSD, Pfizer, Consultant of: Abbvie, Biogen, BMS, Boehringer Ingelheim, Celgene, Lilly, Janssen, Medac, MSD France, Nordic Pharma, Novartis, Pfizer, Roche, Sanofi Aventis, SOBI and UCB, Arsenе Mekinian: None declared, Elodie Regnier: None declared, David Sandroni: None declared, Joe-Elie Salem: None declared, Jérémie Sel-LAM: None declared, Philippe Seksik: None declared, David Klatzmann Consultant of: LTOO Pharma

None declared, Selim Aractangi: None declared, Beatrice Banville Speakers bureau: Lilly, Novartis, Laurent Beaugerie: None declared, Francis Berenbaum Grant/research support from: TRB Chemedica (through institution), MSD (through institution), Pfizer (through institution), Consultant of: Novartis, MSD, Pfizer, Lilly, UCB, Abbvie, Roche, Servier, Sanofi-Aventis, Flexion Therapeutics, Expanscience, GSK, Biogen, Nordic, Sandoz, Regeneron, Gilead, Bone Therapeutics, Regulaxis, Peptinov, 4P Pharma, Paid instructor for: Sandoz, Speakers bureau: Novartis, MSD, Pfizer, Lilly, UCB, Abbvie, Roche, Servier, Sanofi-Aventis, Flexion Therapeutics, Expanscience, GSK, Biogen, Nordic, Sanofi, Pfizer, Gilead, Sandoz, Julien Champey; None declared, Olivier Chazourilles: None declared, Christophe Corpechot: None declared, Bruno Fautrel Grant/research support from: Abbvie, Lilly, MSD, Pfizer, Consultant of: Abbvie, Biogen, BMS, Boehringer Ingelheim, Celgene, Lilly, Janssen, Medac, MSD France, Nordic Pharma, Novartis, Pfizer, Roche, Sanofi Aventis, SOBI and UCB, Arsenе Mekinian: None declared, Elodie Regnier: None declared, David Sandroni: None declared, Joe-Elie Salem: None declared, Jérémie Sel-LAM: None declared, Philippe Seksik: None declared, David Klatzmann Consultant of: LTOO Pharma

Background: In the acute phase of adult-onset Still's disease (AOSD), elevated levels of proinflammatory cytokines (IFN-γ) are shown. Moreover, IFN-γ impacts on activating macrophages which play a crucial role in the pathogenesis of AOSD. Natural killer (NK) cells and T helper cells are in charge of secreting IFN-γ in the innate and adaptive immune systems of disease, respectively. However, the features of their IFN-γ-producing variation depending on disease activity are still uncertain in AOSD;

Objectives: We investigated characteristics of IFN-γ-producing CD4+ T cells and NK cells in patients with AOSD.

Methods: Twenty-four patients in the acute phase of AOSD (active AOSD), 8 of them after treatment (remission), and 12 healthy controls (HC) were recruited in this study. Peripheral blood mononuclear cells and serum samples were provided from them for the experimental analysis. Flow cytometry was used for analyzing CD4+ T cells, CD4+ regulatory T cells (Tregs), NK cells, and their intracellular IFN-γ expression as well as suppression assay of Tregs. The serum concentration of interleukin-18 (IL-18) was measured using commercially available ELISA kit. Relationship between the analyzed data and clinical findings related to disease activity were statistically evaluated.

Results: IFN-γ expression in CD4+ T cells was significantly higher in active AOSD than in HC (p < 0.05). Tregs also significantly indicated higher expression of IFN-γ in active AOSD than in HC (p < 0.0001), and moreover, Tregs were significantly impaired in their suppression ability (p < 0.05). In both CD4+ T cells and Tregs, expression of IFN-γ was significantly correlated with serum ferritin levels in active AOSD (p < 0.05). IFN-γ expression in CD4+ T cells was significantly higher in patients with splenomegaly than those without that (p < 0.05). The proportion of NK cells was significantly lower in active AOSD than in HC (p < 0.0005), whereas IFN-γ expression in NK cells was significantly higher in active AOSD than in HC (p < 0.0005). The number of NK cells and IFN-γ expression in NK cells had inverse relationship with serum ferritin levels in active AOSD (p < 0.05 and p < 0.005, respectively). Increased number of NK cells and their decreased expression of IFN-γ were significantly demonstrated in remission (p < 0.05). In the analyses of NK cell subsets, lower expression of IFN-γ in CD56dim NK cells than in CD56bright NK cells were also observed (p < 0.05). In remission, IFN-γ expression was significantly decreased in CD56dim NK cells (p < 0.05) despite no significant recovery of that in CD56bright NK cells (p = 0.311). Meanwhile, increased expression of IFN-γ in CD56dim NK cells was demonstrated in only patients who were treated with biologics. Although serum levels of IL-18 were significantly higher in active AOSD than in remission and HC; however, they had no significant correlations with any analyzed data.

Conclusion: CD4+ T cells and NK cells promote IFN-γ expression in the acute phase of AOSD. Meanwhile, increased expression of IFN-γ in CD4+ T cells and decreased number of NK cells were correlated with serum ferritin levels, suggesting that they are indicators of disease activity. Furthermore, high disease activity may impact on the alteration of IFN-γ-producing balance in two distinct population of NK cells, and the plasticity of Tregs leading to defect in suppression ability.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1817